Evidence Check
IGSD PSP

13-12-2018

Contents

Introduction

Dear all,

We are very pleased that we have finalized our part of the evidence check. Now we could benefit greatly from your expertise and experiences in the GSD community.

It is quite an extensive document. We ask you to divide task and/or questions as you see fit. You could divide the questions amongst the group, or your could divide tasks (a.k.a. two will look at the evidence, one will look at readability, one on merging of questions).

Please understand that we had to compromise and we were not able to do a complete literature review per question in the available time. We would like for you to add specific knowledge that is essential and will change the core that the question is about.

The best of luck and we are available for any of your questions!

Kind regards,

Willemijn and Fabian

Examples of the Evidence Check

When checking the evidence, first online sources will be reviewed. The choice was made to review the three main accessible databases for medical articles: Pubmed, Web of Science and Embase.
Search strategies based on Mesh terms and Title Abstract searches were made.

Glycogen Storage Disease was used for every search term. The key words of a question and synonyms were used to look for Mesh terms or Title Abstract searches.

Articles before 2001 were not individually mentioned, since they are mostly included in the reviews performed afterwards.

Only articles relevant for liver Glycogen Storage Disease are mentioned in this document. The conclusions of these articles relevant to the question were mentioned. If the question is answered, the question is removed. If the question is not answered, the question remains the same. If the question is partially answered, a suggestion for adapting the question is made.

Workflow Template

We want each group to look over their own questions and the evidence check of the questions. We think that each member of the group can lend their expertise to the evidence check. We propose to evaluate the questions in the following manner:

1. Check whether you agree with the presented evidence of the questions and add articles or your own expertise on the question.
2. Check if you agree with the wording of the final question and if the question is understandable enough for patients, parents and health care professionals and reduced to the core of what the question is about.
3. Check if you agree with questions that are merged and if you think there are any other questions that should/can be merged.

Practically, we have stated for each question
1) what the question before the evidence check was
2) what the search strategy was that we used,
3) which articles we found that were relevant to the question,
4) a short conclusion of the articles,
5) if we think the question is answered, partially answered or not answered or if the question was merged with another, and
6) what the final question could be.
We used a green colour for final questions that are altered, blue if the question is merged and red if we have any remaining remarks for that question.

Search Strategy
Pubmed:

Found articles:

Conclusion of articles:

Summary Question answered:

Final Summary Question:

Please give us back your feedback in the following manner:

1: Code of the Question
2: Additional evidence or expert opinion
3: Remarks on wording of final question
4: Remarks on merging of questions

Example format per question:

Summary Questions Group 1

Code: G1AO1
How should monitoring be performed in adult patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Diseasel"[Mesh] OR "glycogen storage disease"[tiab]) AND "metabolic control"[tiab] AND "Adult"[Mesh]

Found articles:
1. Title: Prevention of complications in glycogen storage disease type Ia with optimization of metabolic control.
Authors: Dambska M, et al.
Year of publication: 2017
PMID:28568353

2. Title: : Progression of renal damage in glycogen storage disease type I is associated to hyperlipidemia: a multicenter prospective Italian study.
Authors: Melis D, et al.
Year of publication: 2016
PMID: 26360666

3. Title: Liver transplantation in glycogen storage disease type I.
Authors: Boers SJ, et al.
Year of publication: 2014
PMID: 24716823

4. Title: Pregnancy in women with glycogen storage disease Ia and Ib
Authors: Ferrecchia IA, et al.
Year of publication: 2014
PMID: 24476649

5. Title: Glycogen storage disease type Ia: linkage of glucose, glycogen, lactic acid, triglyceride and uric acid metabolism
Authors: Sever S, et al.
Year of publications: 2012
PMID: 23312056

6. Title: Dietary dilemmas in the management of glycogen storage disease type I
Authors: Bhattacharya K.
Year of publication: 2011
PMID: 21491105

7.Title: Natural History of hepatocellular adenoma formation in glycogen storage disease type I
Authors: Wang DQ, et al.

Year of publication: 2011
PMID: 21481415

8. Title: An adult male patient with multiple adenomas and a hepatocullular carcinoma: mild glycogen storage disease type Ia.
Authors: Cassiman D, et al.
Year of publication: 2010
PMID: 20447711

9. Title: Glycogen Storage Disease type 1: impact of medium-chain triglycerides on metabolic control and growth.
Authors: Das AM, et al.
Year of publication: 2010
PMID: 20357432

10. Title: Hyperlipidemia in glycogen storage disease type III: effect of age and metabolic control
Authors: Bernier AV
Year of publication: 2008
PMID: 18709545

11. Title: Combined liver-kidney transplantation in glycogen storage disease type Ia: a case beyond the guidelines
Authors: Belingheri M, et al.
Year of publication 2007
PMID: 17457869

12. Title: Bone mineral density in children, adolescents and adults with glycogen storage disease type Ia: a cross-sectional and longitudinal study
Authors: Rake JP, et al.
Year of publication: 2003
PMID: 12971425

13. Title: Type I glycogen storage disease: favourable outcome on a strict management regimen avoiding increased lactate production during childhood and adolescence.
Authors: Däublin G, et al.
Year of publication: 2002
PMID: 12373569

14. Title: Effect of continuous glucose therapy with uncooked cornstarch on the long-term clinical course of type 1a glycogen storage disease
Authors: Weinstein DA, et al.
Year of publication: 2002
PMID: 12373568

Conclusion of articles:

1. There is increasing evidence that complications can be delayed or prevented **with optimal metabolic control** as previously was seen in diabetes.

2. Metabolic control includes monitoring values measured in the blood.

3. Prevention of complications is considered important in adult life (i.e. adenoma, hepatocellular carcinoma, etc).

4. Clinical heterogeneity and disease severity determine outcomes.

5. Pregnancy and other situations that occur in adult life have to be taken into account.

6. How to adjust diet therapy based on monitoring parameters

7. Transplantation indications and the effect on metabolic control should be taken into account.

Summary Question answered:

Partly, based on the abovementioned conclusions. We should specify control into “metabolic control and outcomes”. Perhaps we should use the verb “evaluate” instead of “done” to specify the need for better parameters for follow-up (i.e. biomarkers). This question can be merged with question G1Age2 by adding “at different stages of life” to the summary question.

Final Summary Question:

G1AO1. How can we better monitor metabolic control and outcomes at different stages of life in patients with liver Glycogen Storage Disease?

Code: G1Age1
How is the (natural) progression of liver Glycogen Storage Disease at different stages of life?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("Disease progression"[tiab] OR "Disease progression"[Mesh] OR "Natural course"[tiab] OR "Natural progression"[tiab])

Found articles:
1. Natural history of hepatocellular adenoma formation in glycogen storage disease type I.
Authors: Wang DQ, Fiske LM, Carreras CT, Weinstein DA.
J Pediatr. 2011 Sep;159(3):442-6. doi: 10.1016/j.jpeds.2011.02.031. Epub 2011 Apr 9.
PMID: 21481415

2. Diagnosis and management of glycogen storage disease type I: a practice guideline of the American College of Medical Genetics and Genomics.
Kishnani PS, Austin SL, Abdenur JE, Arn P, Bali DS, Boney A, Chung WK, Dagli AI, Dale D, Koeberl D, Somers MJ, Wechsler SB, Weinstein DA, Wolfsdorf JI, Watson MS; American College of Medical Genetics and Genomics.
Genet Med. 2014 Nov;16(11):e1. PMID: 25356975

3. Systemic progression of type IV glycogen storage disease after liver transplantation.
Willot S, Marchand V, Rasquin A, Alvarez F, Martin SR.
J Pediatr Gastroenterol Nutr. 2010 Nov;51(5):661-4. doi: 10.1097/MPG.0b013e3181d29780.
PMID: 20531024

4. Hepatic glycogen storage disorders: what have we learned in recent years?
Burda P, Hochuli M.
Curr Opin Clin Nutr Metab Care. 2015 Jul;18(4):415-21. doi:
10.1097/MCO.0000000000000181. Review.
PMID: 26001652

5. Glycogen storage disease type 1 and diabetes: learning by comparing and contrasting the two disorders.
Rajas F, Labrune P, Mithieux G.
Diabetes Metab. 2013 Oct;39(5):377-87. doi: 10.1016/j.diabet.2013.03.002. Epub 2013 May 2. Review.PMID: 23643353

6. Does increased fatty acid oxidation enhance development of liver cirrhosis and progression to hepatocellular carcinoma in patients with glycogen storage disease type-III?
Herrema H, Smit GP, Reijngoud DJ, Kuipers F.
J Hepatol. 2007 Aug;47(2):298-300; author reply 300-1. Epub 2007 May 29. No abstract available. PMID: 17570555

7. Glycogen storage disease type III diagnosis and management guidelines.
Kishnani PS, Austin SL, Arn P, Bali DS, Boney A, Case LE, Chung WK, Desai DM, El-Gharbawy A, Haller R, Smit GP, Smith AD, Hobson-Webb LD, Wechsler SB, Weinstein DA, Watson MS; ACMG.
Genet Med. 2010 Jul;12(7):446-63. doi: 10.1097/GIM.0b013e3181e655b6. Erratum in: Genet Med. 2010 Sep;12(9):566.
PMID: 20631546

8. Progression of renal damage in glycogen storage disease type I is associated to hyperlipidemia: a multicenter prospective Italian study.
Melis D, Cozzolino M, Minopoli G, Balivo F, Parini R, Rigoldi M, Paci S, Dionisi-Vici C, Burlina A, Andria G, Parenti G.
J Pediatr. 2015 Apr;166(4):1079-82. doi: 10.1016/j.jpeds.2014.12.015. Epub 2015 Jan 29.
PMID: 25641239

9. Diabetes mellitus associated with glycogen storage disease type III.
Spengos K, Michelakakis H, Vontzalidis A, Zouvelou V, Manta P.
Muscle Nerve. 2009 Jun;39(6):876-7. doi: 10.1002/mus.21201. No abstract available.
PMID: 19334047

10. Glycogen storage disease type III in the Irish population.
Crushell E, Treacy EP, Dawe J, Durkie M, Beauchamp NJ.
J Inherit Metab Dis. 2010 Dec;33 Suppl 3:S215-8. doi: 10.1007/s10545-010-9096-4. Epub 2010 May 20.
PMID: 20490926

11. Liver transplantation in glycogen storage disease type I.
Boers SJ, Visser G, Smit PG, Fuchs SA.
Orphanet J Rare Dis. 2014 Apr 9;9:47. doi: 10.1186/1750-1172-9-47. Review.
PMID: 24716823

12. Preemptive liver-kidney transplantation in von Gierke disease: a case report.
Marega A, Fregonese C, Tulissi P, Vallone C, Gropuzzo M, Toniutto PL, Baccarani U, Bresadola F, Toso F, Montanaro D.
Transplant Proc. 2011 May;43(4):1196-7. doi: 10.1016/j.transproceed.2011.03.003.
PMID: 21620087

13. Glycogenotic hepatocellular carcinoma with glycogen-ground-glass hepatocytes: a heuristically highly relevant phenotype.
Bannasch P.
World J Gastroenterol. 2012 Dec 14;18(46):6701-8. doi: 10.3748/wjg.v18.i46.6701.
PMID: 23239906

14. Branching enzyme deficiency: expanding the clinical spectrum.
Paradas C, Akman HO, Ionete C, Lau H, Riskind PN, Jones DE, Smith TW, Hirano M, Dimauro S.
JAMA Neurol. 2014 Jan;71(1):41-7. doi: 10.1001/jamaneurol.2013.4888.

PMID: 24248152

15. Fifteen years of follow-up of a liver transplant recipient with glycogen storage disease type Ia (Von Gierke disease).
Maya Aparicio AC, Bernal Bellido C, Tinoco González J, Garcia Ruíz S, Aguilar Romero L, Marín Gómez LM, Suárez Artacho G, Alamo Martínez JM, Serrano Díez-Canedo J, Padillo Ruíz FJ, Gomez Bravo MA.
Transplant Proc. 2013;45(10):3668-9. doi: 10.1016/j.transproceed.2013.10.033.
PMID: 24314991

16. A neonatal form of glycogen storage disease type IV.
Nambu M, Kawabe K, Fukuda T, Okuno TB, Ohta S, Nonaka I, Sugie H, Nishino I.
Neurology. 2003 Aug 12;61(3):392-4.
PMID: 12913206

17. Involvement of endocrine system in a patient affected by glycogen storage disease 1b: speculation on the role of autoimmunity.
Melis D, Della Casa R, Balivo F, Minopoli G, Rossi A, Salerno M, Andria G, Parenti G.
Ital J Pediatr. 2014 Mar 19;40(1):30. doi: 10.1186/1824-7288-40-30.
PMID: 24646511

18. Diabetes mellitus secondary to glycogen storage disease type III.
Oki Y, Okubo M, Tanaka S, Nakanishi K, Kobayashi T, Murase T.
Diabet Med. 2000 Nov;17(11):810-2.
PMID: 11131107

19. Renal function in glycogen storage disease type I, natural course, and renopreservative effects of ACE inhibition.
Martens DH, Rake JP, Navis G, Fidler V, van Dael CM, Smit GP.
Clin J Am Soc Nephrol. 2009 Nov;4(11):1741-6. doi: 10.2215/CJN.00050109. Epub 2009 Oct 1. PMID: 19808227

20. Hepatocellular failure in glycogen storage disorder type 3.
Ingle SA, Moulick ND, Ranadive NU, Khedekar K.
J Assoc Physicians India. 2004 Feb;52:158-60.
PMID: 15656054

21. Resection of hepatocellular adenoma in patients with glycogen storage disease type Ia.
Reddy SK, Kishnani PS, Sullivan JA, Koeberl DD, Desai DM, Skinner MA, Rice HE, Clary BM.
J Hepatol. 2007 Nov;47(5):658-63. Epub 2007 Jun 18.
PMID: 17637480

22. Progressive development of renal cysts in glycogen storage disease type I.
Gjorgjieva M, Raffin M, Duchampt A, Perry A, Stefanutti A, Brevet M, Tortereau A, Dubourg L, Hubert-Buron A, Mabille M, Pelissou C, Lassalle L, Labrune P, Mithieux G, Rajas F.

Hum Mol Genet. 2016 Sep 1;25(17):3784-3797. doi: 10.1093/hmg/ddw224. Epub 2016 Jul 19. PMID: 27436577

23. Glycogen storage disease type III-hepatocellular carcinoma a long-term complication?
Demo E, Frush D, Gottfried M, Koepke J, Boney A, Bali D, Chen YT, Kishnani PS.
J Hepatol. 2007 Mar;46(3):492-8. Epub 2006 Nov 9. Review.
PMID: 17196294

24. Neutropenia, neutrophil dysfunction, and inflammatory bowel disease in glycogen storage disease type Ib: results of the European Study on Glycogen Storage Disease type I.
Visser G, Rake JP, Fernandes J, Labrune P, Leonard JV, Moses S, Ullrich K, Smit GP.
J Pediatr. 2000 Aug;137(2):187-91.
PMID: 10931410

25. Cross-sectional retrospective study of muscle function in patients with glycogen storage disease type III.
Decostre V, Laforêt P, Nadaj-Pakleza A, De Antonio M, Leveugle S, Ollivier G, Canal A, Kachetel K, Petit F, Eymard B, Behin A, Wahbi K, Labrune P, Hogrel JY.
Neuromuscul Disord. 2016 Sep;26(9):584-92. doi: 10.1016/j.nmd.2016.06.460. Epub 2016 Jun 28.
PMID: 27460348

26. Liver glycogenosis as early manifestation in type 1 diabetes mellitus.
Carcione L, Lombardo F, Messina MF, Rosano M, De Luca F.
Diabetes Nutr Metab. 2003 Jun;16(3):182-4.
PMID: 14635736

27. The natural history of glycogen storage disease types VI and IX: Long-term outcome from the largest metabolic center in Canada.
Roscher A, Patel J, Hewson S, Nagy L, Feigenbaum A, Kronick J, Raiman J, Schulze A, Siriwardena K, Mercimek-Mahmutoglu S.
Mol Genet Metab. 2014 Nov;113(3):171-6. doi: 10.1016/j.ymgme.2014.09.005. Epub 2014 Sep 21. PMID: 25266922

Conclusion of articles:

1. Complications (renal, cardial, hepatic, muscle) are an important focus of the research into the natural history of liver GSD. The pathophysiology / mechanism is incompletely understood.
2. There is a difference in natural course of the disease and the course after an intervention has taken place.
3. For GSD I and III there are extensive guidelines available, but not for other liver GSD types. The articles on the other liver GSD types are mostly case series.
4. Age of onset is important for the natural course of liver GSD.
5. Especially data on the ageing population is few in number.
6. General remark: many larger cohort studies include patients from Europe and the US/Canada, but other continents are underrepresented.

Summary Question answered:
No, there is still lacks of knowledge for the ageing population, non-GSD I or III types and patients not from Europe or the US.
The differences between natural course and course after interventions are described in other questions, mostly the summary questions on complications.

Final Summary Question:

Same:

How is the (natural) progression of liver Glycogen Storage Disease at different stages of life?

Code: G1Age2

How is the management and monitoring of patients with liver Glycogen Storage Disease at different stages of life?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

See also the articles and conclusions from G1AO1

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("metabolic control"[tiab] OR "monitoring"[tiab])

Found articles:
See G1AO1

Conclusion of articles:

Same as G1AO1

Summary Question answered:

Partly. This question can be merged with question G1AO1 by adding “at different stages of life" to the summary question.

Final Summary Question:

None.

Code: G1CC1
How can all healthcare providers involved (including experts) contribute to shared care for individual patients with liver Glycogen Storage Disease

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("Precision Medicine"[Mesh] OR "precision medicine"[tiab] OR "individual"[tiab] OR "shared care"[tiab])

Found articles:
1. A preliminary study of telemedicine for patients with hepatic glycogen storage disease and their healthcare providers: from bedside to home site monitoring.
Hoogeveen IJ, Peeks F, de Boer F, Lubout CMA, de Koning TJ, Te Boekhorst S, Zandvoort RJ, Burghard R, van Spronsen FJ, Derks TGJ.
J Inherit Metab Dis. 2018 Mar 29. doi: 10.1007/s10545-018-0167-2. [Epub ahead of print]
PMID: 29600495

2. Hepatic Glycogen Storage Diseases, Terry G. J. Derks, et al.
First Published September 26, 2017 Research Article
https://doi.org/10.1177/2326409817733009

Conclusion of articles:
1. Shared care can be improved by telemedicine platforms in which patients and healthcare professionals can share data.
2. Patient participation is important for shared care.
3. International collaboration via telemedicine platforms, conferences, etc. can contribute to shared care.

Summary Question answered:
No. There have been some suggestions for how healthcare providers can contribute to shared care, but these are first implementations or suggestions.

Final Summary Question:

Same:

How can all healthcare providers involved (including experts) contribute to shared care for individual patients with liver Glycogen Storage Disease?

Code: G1Car1

What is the relationship between carriership of liver Glycogen Storage Disease and symptoms and signs?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:

("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("Heterozygote"[Mesh] OR "Heterozygote"[tiab] OR "Carrier*"[tiab]) AND ("symptom*"[tiab] OR "sign*"[tiab])

Found articles:

1. Synergistic heterozygosity: disease resulting from multiple partial defects in one or more metabolic pathways.
Vockley J, Rinaldo P, Bennett MJ, Matern D, Vladutiu GD.
Mol Genet Metab. 2000 Sep-Oct;71(1-2):10-8. Review.
PMID: 11001791

2. Manifesting heterozygotes in McArdle's disease: clinical, morphological and biochemical studies in a family.
Manfredi G, Silvestri G, Servidei S, Ricci E, Mirabella M, Bertini E, Papacci M, Rana M, Tonali P.
J Neurol Sci. 1993 Mar;115(1):91-4.
PMID: 8468596

Conclusion of articles:

1. Carriers could possibly have a manifestation of symptoms due to a synergistic effect of partial genetic defects. The GSD-carriers may have a second mutation in another part of the glycogen metabolism, which has not been systematically addressed in literature.
2. In GSD V there have been reports of heterozygotes manifesting clinical symptoms at an enzyme activity of 30-50%. Therefore, it may be a valid question for liver GSD.

Summary Question answered:

No, this question has not been answered for liver GSD.

Final Summary Question:

Same

What is the relationship between carriership of liver Glycogen Storage Disease and symptoms and signs?

Code: G1DP1
How can we improve the diagnostic procedures for patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("Diagnosis"[Mesh] OR "Diagnosis"[tiab]) NOT ("Glycogen Storage Disease Type II"[Mesh])

Found articles:
Many articles focus on diagnostic procedure. Because there were a lot of articles on GSD II, we added the Mesh term to exclude GSD II. An overview of the most important reviews:

1. Inborn Errors of Metabolism with Hypoglycemia: Glycogen Storage Diseases and Inherited Disorders of Gluconeogenesis.
Weinstein DA, Steuerwald U, De Souza CFM, Derks TGJ.
Pediatr Clin North Am. 2018 Apr;65(2):247-265. doi: 10.1016/j.pcl.2017.11.005. **Review**.

PMID: 29502912

2. **Glycogen Storage Disease**.
Stone WL, Adil A.
StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-.
2017 Oct 14.

PMID: 2908378

3. **Glycogen storage disease** type III **diagnosis** and management guidelines.
Kishnani PS, Austin SL, Arn P, Bali DS, Boney A, Case LE, Chung WK, Desai DM, El-Gharbawy A, Haller R, Smit GP, Smith AD, Hobson-Webb LD, Wechsler SB, Weinstein DA, Watson MS; ACMG.
Genet Med. 2010 Jul;12(7):446-63. doi: 10.1097/GIM.0b013e3181e655b6. Erratum in: Genet Med. 2010 Sep;12(9):566.
PMID: 20631546

4. Tophaceous gout in a female premenopausal patient with an unexpected **diagnosis** of **glycogen storage disease** type Ia: a case report and literature **review**.
Zhang B, Zeng X.
Clin Rheumatol. 2016 Nov;35(11):2851-2856. Epub 2016 May 2. **Review**.

PMID: 27139513

5. Using human-induced pluripotent stem cells to model monogenic metabolic disorders of the liver.
Ordonez MP, Goldstein LS.
Semin Liver Dis. 2012 Nov;32(4):298-306. doi: 10.1055/s-0032-1329898. Epub 2013 Feb 8. **Review**.

PMID: 23397530

6. Hypoglycaemia related to inherited metabolic diseases in adults.
Douillard C, Mention K, Dobbelaere D, Wemeau JL, Saudubray JM, Vantyghem MC.
Orphanet J Rare Dis. 2012 May 15;7:26. doi: 10.1186/1750-1172-7-26. **Review**.
PMID: 22587661

7. Glycogen storage diseases: a brief **review** and update on clinical features, genetic abnormalities, pathologic features, and treatment.
Hicks J, Wartchow E, Mierau G.
Ultrastruct Pathol. 2011 Oct;35(5):183-96. doi: 10.3109/01913123.2011.601404. **Review**.
PMID: 21910565

8. Inborn errors of carbohydrate metabolism.
Mayatepek E, Hoffmann B, Meissner T.
Best Pract Res Clin Gastroenterol. 2010 Oct;24(5):607-18. doi: 10.1016/j.bpg.2010.07.012. **Review**.
PMID: 20955963

9. **Glycogen storage disease** type I: indications for liver and/or kidney transplantation.
Labrune P.
Eur J Pediatr. 2002 Oct;161 Suppl 1:S53-5. Epub 2002 Jul 19. **Review**.
PMID: 12373572

10. The variable presentations of **glycogen storage disease** type IV: a **review**of clinical, enzymatic and molecular studies.
Moses SW, Parvari R.
Curr Mol Med. 2002 Mar;2(2):177-88. **Review**.
PMID:11949934

11. **Glycogen storage disease** type Ia: recent experience with mutation analysis, a summary of mutations reported in the literature and a newly developed diagnostic flow chart.
Rake JP, ten Berge AM, Visser G, Verlind E, Niezen-Koning KE, Buys CH, Smit GP, Scheffer H.
Eur J Pediatr. 2000 May;159(5):322-30. **Review**.
PMID: 10834516

12. **Glycogen storage disease** type III with muscle involvement: reappraisal of phenotypic variability and prognosis.
Momoi T, Sano H, Yamanaka C, Sasaki H, Mikawa H.
Am J Med Genet. 1992 Mar 1;42(5):696-9. **Review**.
PMID: 1632441

13. Elevated serum biotinidase activity in hepatic glycogen storage disorders--a convenient **biomarker**.
Paesold-Burda P, Baumgartner MR, Santer R, Bosshard NU, Steinmann B.
J Inherit Metab Dis. 2007 Nov;30(6):896-902. Epub 2007 Nov 12.
PMID: 17994282

Conclusion of articles:

1. An important aspect of diagnosis is early recognition of symptoms and signs. These symptoms are not clear to all healthcare professionals and for this close history taking and pattern recognition are important.

2. There are cases in which liver GSD is diagnosed in adulthood with other than typical presenting symptoms, which need further examination.

3. There are few available biomarkers that are sensitive and specific for liver Glycogen Storage Diseases. Further biomarkers are discussed (such as biotinidase and tetrasaccharide).

4. For diagnosis, it is important to take heterogeneity in phenotype for liver Glycogen Storage Diseases into account. Several models to study heterogeneity are discussed, such as stem cell models.

5. There are multiple articles that specify about diagnostic procedure of complications regarding liver Glycogen Storage Diseases.

Summary Question answered:
Partly. There has been a lot of work into the diagnostic process of liver GSD. Still there are cases that are missed and biomarkers that should be further evaluated. Since other questions already focus on biomarkers, phenotype and diagnostic procedure of complications, we should specify that this summary questions is about diagnosis of liver GSD, since this can also focus on prenatal diagnosis, etc.

Final Summary Question:

How can we improve the diagnostic procedures of liver Glycogen Storage Disease?

Code: G1DS1

Is there a way of better understanding severity levels between different patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:

("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("Disease severity"[tiab] OR "Heterogeneity"[tiab] OR "Phenotype"[tiab]) NOT ("Glycogen Storage Disease Type II"[Mesh])

Found articles:

1. Type I glycogen storage diseases: disorders of the glucose-6-phosphatase/glucose-6-phosphate transporter complexes.
Chou JY, Jun HS, Mansfield BC.
J Inherit Metab Dis. 2015 May;38(3):511-9. doi: 10.1007/s10545-014-9772-x. Epub 2014 Oct 7. Review.

PMID: 25288127

2. **Glycogen storage disease** type III: the **phenotype** branches out.
Haller RG.
Neurology. 2015 Apr 28;84(17):1726-7. doi: 10.1212/WNL.0000000000001532. Epub 2015 Apr 1. No abstract available.

PMID: 25832667

3. **Glycogen storage disease** type 1b: Mild **phenotype** associated with a novel splice site mutation.
Chopra M, Jackson R, Durkie M, Beauchamp NJ, Kirk EP.
Mol Genet Metab. 2009 Aug;97(4):315. doi: 10.1016/j.ymgme.2009.04.012. Epub 2009 May 3. No abstract available.

PMID: 19454374

4. **Glycogen storage disease** type III in the Irish population.
Crushell E, Treacy EP, Dawe J, Durkie M, Beauchamp NJ.
J Inherit Metab Dis. 2010 Dec;33 Suppl 3:S215-8. doi: 10.1007/s10545-010-9096-4. Epub 2010 May 20.
PMID: 20490926

5. The variable clinical **phenotype** of liver glycogen synthase deficiency.
Spiegel R, Mahamid J, Orho-Melander M, Miron D, Horovitz Y.
J Pediatr Endocrinol Metab. 2007 Dec;20(12):1339-42.

PMID: 18341095

6. Hypercalcemia in **glycogen storage disease** type I patients of Turkish origin.
Kasapkara CS, Tümer L, Okur I, Eminoğlu T, Ezgü FS, Hasanoğlu A.
Turk J Pediatr. 2012 Jan-Feb;54(1):35-7.

PMID:22397040

7. **Glycogen storage disease** type I: diagnosis and **phenotype**/genotype correlation.
Matern D, Seydewitz HH, Bali D, Lang C, Chen YT.
Eur J Pediatr. 2002 Oct;161 Suppl 1:S10-9. Epub 2002 Jul 27.

PMID: 12373566

8. A case of **glycogen storage disease** type III (glycogen debranching enzyme deficiency) with liver cirrhosis and hypertrophic cardiomyopathy.
Kobayashi A, Nishinomiya F, Fukamachi Y, Ohtaka M, Yamamoto J, Takagi K, Tanaka S, Takizawa S, Imadachi H, Fukase M, et al.
Tohoku J Exp Med. 1995 Jul;176(3):181-5.

PMID: 8553356

9. **Glycogen storage disease** type IV: novel mutations and molecular characterization of a heterogeneous disorder.
Li SC, Chen CM, Goldstein JL, Wu JY, Lemyre E, Burrow TA, Kang PB, Chen YT, Bali DS.
J Inherit Metab Dis. 2010 Dec;33 Suppl 3:S83-90. doi: 10.1007/s10545-009-9026-5. Epub 2010 Jan 8.
PMID: 20058079

10. **Glycogen storage disease**: clinical, biochemical, and molecular **heterogeneity**.
Shin YS.
Semin Pediatr Neurol. 2006 Jun;13(2):115-20. Review.

PMID: 17027861

11. Genotype-**phenotype** correlation in two frequent mutations and mutation update in type III **glycogen storage disease**.
Shaiu WL, Kishnani PS, Shen J, Liu HM, Chen YT.
Mol Genet Metab. 2000 Jan;69(1):16-23.

PMID: 10655153

12. Genotype/**phenotype** correlation in **glycogen storage disease** type 1b: a multicentre study and review of the literature.
Melis D, Fulceri R, Parenti G, Marcolongo P, Gatti R, Parini R, Riva E, Della Casa R, Zammarchi E, Andria G, Benedetti A.
Eur J Pediatr. 2005 Aug;164(8):501-8. Epub 2005 May 19. Review.

PMID: 15906092

13. Branching enzyme deficiency/glycogenosis storage disease type IV presenting as a severe congenital hypotonia: muscle biopsy and autopsy findings, biochemical and molecular genetic studies.
Taratuto AL, Akman HO, Saccoliti M, Riudavets M, Arakaki N, Mesa L, Sevlever G, Goebel H, DiMauro S.
Neuromuscul Disord. 2010 Dec;20(12):783-90. doi: 10.1016/j.nmd.2010.07.275. Epub 2010 Sep 15.
PMID: 20833045

14. The variable presentations of **glycogen storage disease** type IV: a review of clinical, enzymatic and molecular studies.
Moses SW, Parvari R.

Curr Mol Med. 2002 Mar;2(2):177-88. Review.
PMID: 11949934

15. **Glycogen storage disease** type Ia: recent experience with mutation analysis, a summary of mutations reported in the literature and a newly developed diagnostic flow chart.
Rake JP, ten Berge AM, Visser G, Verlind E, Niezen-Koning KE, Buys CH, Smit GP, Scheffer H.
Eur J Pediatr. 2000 May;159(5):322-30. Review.

PMID: 10834516

16. Clinical and genetic **heterogeneity** of branching enzyme deficiency (glycogenosis type IV).
Bruno C, van Diggelen OP, Cassandrini D, Gimpelev M, Giuffrè B, Donati MA, Introvini P, Alegria A, Assereto S, Morandi L, Mora M, Tonoli E, Mascelli S, Traverso M, Pasquini E, Bado M, Vilarinho L, van Noort G, Mosca F, DiMauro S, Zara F, Minetti C.
Neurology. 2004 Sep 28;63(6):1053-8.

PMID: 15452297

17. Mutation Analysis in **Glycogen Storage Disease** Type III Patients in the Netherlands: Novel Genotype-**Phenotype** Relationships and Five Novel Mutations in the AGL Gene.
Sentner CP, Vos YJ, Niezen-Koning KN, Mol B, Smit GP.
JIMD Rep. 2013;7:19-26. doi: 10.1007/8904_2012_134. Epub 2012 Mar 16.

PMID: 23430490

18. Clinical and biochemical **heterogeneity** between patients with **glycogen storage disease** type IA: the added value of CUSUM for metabolic control.
Peeks F, Steunenberg TAH, de Boer F, Rubio-Gozalbo ME, Williams M, Burghard R, Rajas F, Oosterveer MH, Weinstein DA, Derks TGJ.
J Inherit Metab Dis. 2017 Sep;40(5):695-702. doi: 10.1007/s10545-017-0039-1. Epub 2017 Apr 10.

PMID: 28397058

19. **Glycogen storage disease** type Ia mice with less than 2% of normal hepatic glucose-6-phosphatase-α activity restored are at risk of developing hepatic tumors.
Kim GY, Lee YM, Kwon JH, Cho JH, Pan CJ, Starost MF, Mansfield BC, Chou JY.
Mol Genet Metab. 2017 Mar;120(3):229-234. doi: 10.1016/j.ymgme.2017.01.003. Epub 2017 Jan 10.

PMID: 28096054

Conclusion of articles:

1. Disease severity in liver GSD has been associated with differences in mutation, enzyme activity and enzyme activity (internal factors). Many molecular and genetic studies have been performed to identify underlying disease severity. For most GSD subtypes, there is not a clear genotype/phenotype correlation.

2. Furthermore, differences in diet and country of origin are two factors that externally could influence phenotype.

3. It is important to focus in finding out which liver GSD patients develop complications under which conditions.

4. International registries are warranted to identify factors that influence disease severity in larger groups of liver GSD patients.

Summary Question answered:
Partly, there have been studies that identify specific parts of the disease severity of liver GSD. There are ways to better understand different severity levels based on clinical, biochemical, environmental, mutational, enzymatic factors. But these have not been studies for all liver GSD types and these could be systematically registered and studied for larger populations.

Final Summary Question:

Changed

How can we better understand differences in disease severity between patients with liver

Glycogen storage disease?

Code: G1E1
What are costs and effects of ongoing care for patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("Health Care Costs"[Mesh] OR "costs"[tiab])

Found articles:
There are no articles related to healthcare costs for liver glycogen storage diseases. Therefore we included articles that are focussed on healthcare costs and muscle glycogen storage diseases.

1. The role of respiratory management of Pompe disease.
Ambrosino N, Confalonieri M, Crescimanno G, Vianello A, Vitacca M.
Respir Med. 2013 Aug;107(8):1124-32. doi: 10.1016/j.rmed.2013.03.004. Epub 2013 Apr 12. Review.

PMID: 23587901

2. Cost-effectiveness of enzyme replacement therapy with alglucosidase alfa in classic-infantile patients with Pompe disease.
Kanters TA, Hoogenboom-Plug I, Rutten-Van Mölken MP, Redekop WK, van der Ploeg AT, Hakkaart L.
Orphanet J Rare Dis. 2014 May 16;9:75. doi: 10.1186/1750-1172-9-75.

PMID: 24884717

3. Newborn screening for pompe disease? a qualitative study exploring professional views.
van El CG, Rigter T, Reuser AJ, van der Ploeg AT, Weinreich SS, Cornel MC.
BMC Pediatr. 2014 Aug 14;14:203. doi: 10.1186/1471-2431-14-203.

PMID: 25124044

4. The cost-effectiveness of enzyme replacement therapy (ERT) for the infantile form of Pompe disease: comparing a high-income country's approach (England) to that of a middle-income one (Colombia).
Castro-Jaramillo HE.
Rev Salud Publica (Bogota). 2012 Jan-Feb;14(1):143-55.

PMID: 23250322

5. Rapid screening of 12 common mutations in Turkish GSD 1a patients using electronic DNA microarray.
Eminoglu TF, Ezgu FS, Hasanoglu A, Tumer L.
Gene. 2013 Apr 15;518(2):346-50. doi: 10.1016/j.gene.2012.12.104. Epub 2013 Jan 23.
PMID: 2335279

6. Joint SOGC-CCMG Opinion for Reproductive Genetic Carrier Screening: 7. An Update for

All Canadian Providers of Maternity and Reproductive Healthcare in the Era of Direct-to-Consumer Testing.
Wilson RD, De Bie I, Armour CM, Brown RN, Campagnolo C, Carroll JC, Okun N, Nelson T, Zwingerman R, Audibert F, Brock JA, Brown RN, Campagnolo C, Carroll JC, De Bie I, Johnson JA, Okun N, Pastruck M, Vallée-Pouliot K, Wilson RD, Zwingerman R, Armour C, Chitayat D, De Bie I, Fernandez S, Kim R, Lavoie J, Leonard N, Nelson T, Taylor S, Van Allen M, Van Karnebeek C.
J Obstet Gynaecol Can. 2016 Aug;38(8):742-762.e3. doi: 10.1016/j.jogc.2016.06.008.

PMID: 27638987

Conclusion of articles:
1. Healthcare costs are not researched in liver Glycogen storage disease.

2. Novel technologies for treatment, such as gene therapy, enzyme replacement therapy, and diagnosis, such as newborn screening and DNA analysis, may warrant an evaluation of healthcare costs.

3. The costs do not only relate to individual patients with liver Glycogen storage disease, but also to their families (family support, carrier screening) and to society as a whole and hence, reflects solidarity

Summary Question answered:
No, there have been studies into healthcare costs, but not in the field of liver glycogen storage diseases. The costs for families of patients with liver Glycogen storage diseases should be included.

Final Summary Question:

Changed

What are costs and effects of healthcare for patients with liver Glycogen Storage Disease and their families?

Code: G1CW1

How important is climate/weather for patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND
("Climate"[Mesh] OR Climate"[tiab] OR “Weather”[Mesh] OR “Weather”[tiab].

Search Strategy Web of Science
TOPIC (climate) AND TOPIC: (glycogen storage disease).

Search Strategy Embase
'glycogen storage disease'/exp AND ‘climate’/exp

Found articles:
None.

Conclusion of articles:
None.

Summary Question answered:
No.

Final Summary Question:

Same:
How important is climate/weather for patients with liver Glycogen Storage Disease?

G1Gen1 **How can we improve genetic counseling for families of patients with liver Glycogen Storage Disease?**

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("Genetic Counseling"[Mesh] OR "Genetic Counseling"[tiab] OR “Preconception Care”[Mesh] OR “Preconception Care”[tiab])

Search Strategy Web of Science:
(TOPIC: (genetic counseling) OR TOPIC: (preconception care)) AND TOPIC: (glycogen storage disease)

Search Strategy Embase:
'glycogen storage disease'/exp AND ('family'/exp OR 'genetic counseling'/exp OR ‘preconception care’/exp).

Found articles:
1. Title: Glycogen Storage Disease: A basic understanding and Guide to Nursing Care
Authors: Triomphe TJ, et al.
Year of publication: 1997
PMID: 9271885

Conclusion of articles:
1. Much is known about the inheritance of Glycogen Storage Diseases.
2. Preconception care is another important term besides genetic counselling.
3. Who performs the genetic counselling for patients with liver Glycogen Storage Disease?
4. Not only families might benefit from genetic counselling, but also the patients themselves (if partner of patient is a carrier).

Summary Question answered:
No. Perhaps we should add preconceptive care to the Summary Question. Perhaps we should specify that also individual patients can be involved, apart from their families.

Final Summary Question:

Same

How can we improve genetic counseling and preconception care for patients and families with liver Glycogen Storage Disease?

Code: G1Inc1
How prevalent is liver Glycogen Storage Disease worldwide?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("Epidemiology"[Mesh] OR "Epidemiology"[tiab] OR "Prevalence"[Mesh] OR "Prevalence"[tiab] OR "Incidence"[Mesh] OR "Incidence"[tiab]) NOT "glycogen storage disease type II"[mesh]

Found articles:
1. **Glycogen storage disease** type I in Tunisia: an epidemiological analysis.
Ben Chehida A, Tebib N, Cherif W, Ben Turkia H, Abdelmoula S, Azzouz H, Ben Dridi MF.
J Inherit Metab Dis. 2008 Dec;31 Suppl 2:S199-204. doi: 10.1007/s10545-008-0707-2. Epub 2008 Aug 5.

PMID: 18679824

2. **Incidence** of **glycogen storage disease** in Sweden.
Ockerman PA.
Acta Paediatr Scand. 1972 Sep;61(5):533-5. No abstract available.

PMID: 4506220

3. Seizures and epilepsy in hypoglycaemia caused by inborn errors of metabolism.
Gataullina S, Delonlay P, Lemaire E, Boddaert N, Bulteau C, Soufflet C, Laín GA, Nabbout R, Chiron C, Dulac O.
Dev Med Child Neurol. 2015 Feb;57(2):194-9. doi: 10.1111/dmcn.12574. Epub 2014 Aug 22.
PMID: 25145506

4. A founder AGL mutation causing **glycogen storage disease** type IIIa in Inuit identified through whole-exome sequencing: a case series.
Rousseau-Nepton I, Okubo M, Grabs R; FORGE Canada Consortium, Mitchell J, Polychronakos C, Rodd C.
CMAJ. 2015 Feb 3;187(2):E68-73. doi: 10.1503/cmaj.140840. Epub 2015 Jan 19.

PMID: 25602008

5. [Three congenital metabolic diseases in the Faeroe Islands. **Incidence**, clinical and molecular genetic characteristics of Faeroese children with **glycogen storage disease** type IIIA, carnitine transporter deficiency and holocarboxylase synthetase deficiency].
Joensen F, Steuerwald EU, Rasmussen NH.
Ugeskr Laeger. 2006 Feb 13;168(7):667-70. Review. Danish.

PMID: 16494802

6. Molecular genetic basis and **prevalence** of **glycogen storage disease** type IIIA in the Faroe Islands.
Santer R, Kinner M, Steuerwald U, Kjaergaard S, Skovby F, Simonsen H, Shaiu WL, Chen YT, Schneppenheim R, Schaub J.
Eur J Hum Genet. 2001 May;9(5):388-91.

PMID: 11378828

7. **Glycogen storage disease** type III in Inuit children.
Zimakas PJ, Rodd CJ.
CMAJ. 2005 Feb 1;172(3):355-8.

PMID: 15684118

8. Mutation frequencies for **glycogen storage disease** Ia in the Ashkenazi Jewish population.
Ekstein J, Rubin BY, Anderson SL, Weinstein DA, Bach G, Abeliovich D, Webb M, Risch N.
Am J Med Genet A. 2004 Aug 30;129A(2):162-4.

PMID: 15316959

9. **Glycogen storage disease** type Ia: frequency and clinical course in Turkish children.
Saltik IN, Ozen H, Ciliv G, Koçak N, Yüce A, Gürakan F, Dinler G.
Indian J Pediatr. 2000 Jul;67(7):497-501.

PMID: 10957834

10. Glucose-6-phosphatase gene mutations in Taiwan Chinese patients with **glycogen storage disease** type Ia.
Chiang SC, Lee YM, Chang MH, Wang TR, Ko TM, Hwu WL.
J Hum Genet. 2000;45(4):197-9.

PMID: 10944847

11. Mutation Spectrum and Birth **Prevalence** of Inborn Errors of Metabolism among Emiratis: A study from Tawam Hospital Metabolic Center, United Arab Emirates.
Al-Shamsi A, Hertecant JL, Al-Hamad S, Souid AK, Al-Jasmi F.
Sultan Qaboos Univ Med J. 2014 Feb;14(1):e42-9. Epub 2014 Jan 27.

PMID: 24516753

12. **Incidence** of inborn errors of metabolism in British Columbia, 1969-1996.
Applegarth DA, Toone JR, Lowry RB.
Pediatrics. 2000 Jan;105(1):e10.
PMID: 10617747

13. **Molecular genetics** of **type 1 glycogen storage disease**.
Janecke AR, Mayatepek E, Utermann G.
Mol Genet Metab. 2001 Jun;73(2):117-25. Review.
PMID: 11386847

14. **Type** I **glycogen storage diseases**: **disorders** of the **glucose-6-phosphatase complex**.
Chou JY, Matern D, Mansfield BC, Chen YT.
Curr Mol Med. 2002 Mar;2(2):121-43. Review.

PMID: 11949931

15. A single-base deletion in the 3'-coding region of glycogen-debranchingenzyme is prevalent in glycogen storage disease type IIIA in a population of North African Jewish patients. Parvari REur J Hum Genet. 1997 Sep-Oct;5(5):266-70. PMID: 9412782

16. Glycogen storage disease. Chen Y. In: Scriver CR, Beaudet AS, Sly WS, Valle D, Childs B, Kinzler KW, Vogelstein B, eds. The Metabolic and Molecular Basis of Inherited Disease. 8 ed. New York, NY: McGraw-Hill; 2001:1521-51

17. Identification of a mutation in liver glycogen phosphorylase in glycogen storage disease type VI. Chang S, Rosenberg MJ, Morton H, Francomano CA, Biesecker LG. Hum Mol Genet. 1998;7:865–70.

Conclusion of articles:

1. Epidemiological studies have been performed in specific countries (Turkey, Emirates, UK) and specific populations (Inuit, Ashketazi Jews).

2. There are suggestions of underreporting or underdiagnoses leading to death before a diagnosis can be made. Furthermore, GSD VI and GSD IX are milder and may lead to underdiagnoses due to their mild nature.

Summary Question answered:

No. There are certain studies in larger cohorts (EGSDI, ISGSDIII) and in country and population specific studies, but there is no general acceptance of the worldwide incidence. I suggest that we change the wording to make the question more readable and add “incidence” to the question to be more correct in an epidemiological sense.

Final Summary Question:

What is the worldwide frequency (prevalence and incidence) of liver Glycogen Storage Disease?

Code: G1Ind1

How best we can help families of patients with liver Glycogen Storage Disease to encourage patients' independency?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:

("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND "independency[tiab]

Found articles:

1. Dietary dilemmas in the management of **glycogen storage disease** type I.
Bhattacharya K.
J Inherit Metab Dis. 2011 Jun;34(3):621-9. doi: 10.1007/s10545-011-9322-8. Epub 2011 Apr 14. Review.

PMID: 21491105

2. Psychosocial functioning in youth with **glycogen storage disease** type I.
Storch E, Keeley M, Merlo L, Jacob M, Correia C, Weinstein D.
J Pediatr Psychol. 2008 Aug;33(7):728-38. doi: 10.1093/jpepsy/jsn017. Epub 2008 Feb 23.

PMID: 18296725

3. Promoting adherence to medical treatment in chronic childhood illness: Concepts, methods, and interventions, Drotar, 2000

4. Safety issues associated with dietary management in patients with hepatic glycogen storage disease. Steunenberg TAH, Peeks, F, et al. Mol Genet Metab. 2018 Sep;125(1-2):79-85. doi: 10.1016/j.ymgme.2018.07.004. Epub 2018 Jul 18.

Conclusion of articles:

1. Parents of GSD youth indicate that they have difficulty functioning independently with regards to the medical regimen, money, budget, shopping, than healthy children.
2. Suggestions were given for professional assistance to determine appropriate opportunities for the youth to participate in activities independently. This is also important to prevent that parents are overly protective.
3. There is a discrepancy between the patient's perspective on safety of dietary management and occurrence of complications as a result of dietary management.

Summary Question answered:

No. A small suggestion for textual change has been made.

Final Summary Question:

Changed

How can we help (families of) patients with liver Glycogen Storage Disease to encourage patients' independency?

Code: G1AD1
What are the consequences of consumption of alcohol and drugs for patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("Alcohols"[Mesh] OR "Alcohol*"[tiab] OR "Street Drugs"[Mesh] OR "Drug*"[tiab])

Found articles:
1. Cocaine toxicity in **glycogen storage disease**.
Wilson BE, Hobbs WN.
West J Med. 1993 Oct;159(4):508-9. No abstract available.

PMID: 8273352

2. THE PARADOXICAL EFFECT OF ALCOHOL ON CARBOHYDRATE METABOLISM IN FOUR PATIENTS WITH LIVER GLYCOGEN DISEASE. LOWE CU, MOSOVICH LL. Pediatrics. 1965 Jun;35:1005-8. PMID: 14296409

Conclusion of articles:
1. In GSD IIIa cocaine has caused rhabdomyolysis and pulmonary edema.
2. Alcohol leads to an increased production of lactate and secondly an inhibition of several steps in the gluconeogenesis.

Summary Question answered:
No. Only several (old) case studies have shown the negative effects of consumption of cocaine and alcohol. There is no study on alcohol and drug consumption on a larger scale. Therefore we suggest to add the consummation of alcohol and drugs to the question.

Final Summary Question:

The same:

What are the consequences of consumption of alcohol and drugs for patients with liver Glycogen Storage Disease?

Code: G1MF1
Should care be differentiated between male and female with the same mutation(s) of patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("Male"[tiab] OR "Female*"[tiab] OR "Gender"[tiab] OR "Sex*"[tiab])

Found articles:

1. Title: Hypogonadotropic Hypogonadism in Males with Glycogen Storage Disease Type 1.
   Authors: Wong EM[1], Lehman A[2], Acott P[3], Gillis J[4], Metzger DL[5], Sirrs S[6,7].
   Year of publication: 2017
   DOI: 10.1007/8904_2016_38.
2. Title: Pregnancy in women with glycogen storage disease type Ia and Ib.
   Authors: Ferrecchia IA, et al.
   Year of publication: 2014.
   PMID: 24476649
3. Title: Fertility and Pregnancy in women affected by glycogen storage disease type I, results of a multicenter Italian study.
   Authors: Sechi A, et al.
   Year of publication: 2013
   PMID: 22562700

Conclusion of articles:
1. In general, there are many case reports on either male or female GSD Ia patients, but not in the form of a comparison. Furthermore, perhaps this research should not be limited to patients with the same mutation, but also to the more general case of females and males in general.

2. Specific notes of difference between female and male care are mentioned with regards to for example pregnancy and hormone levels.

Summary Question answered:
No. A small textual change has been added.

Final Summary Question:

Changed:

Should care be differentiated between male and female patients (with the same mutations)

with liver Glycogen Storage Disease?

Code: G1Mon2
What are the alarm symptoms of patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("alarm symptoms"[tiab])

Found articles:
None.

Conclusion of articles:
This is a very general summary question. We could interpret alarm symptoms as symptoms for hypoglycaemia and metabolic derangement, as presenting symptoms, as symptoms that are present when complications occur. These have been identified in large part for GSD Ia, Ib and III. However, larger studies for the rarer GSD types are not present. Specific symptoms that occur during alarm symptoms are discussed, but not in a systematic way. Furthermore, this question does not focus on the absence of alarm symptoms.

Summary Question answered:
No. I propose to add “how can we identify them” to focus also on detection of symptoms.

Final Summary Question:

Changed:

What are the alarm symptoms of patients with liver Glycogen Storage Disease and how can they be recognized?

Code: G1Mon3

Do we need new methods for monitoring metabolic control (like noninvasive continuous glucose and lactate measurements, new biomarkers) for patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "glycogen storage disease"[tiab]) AND ("metabolic control"[tiab] OR "biomarkers"[tiab] OR "monitoring"[tiab].

Found articles:

1. Impaired bone metabolism in glycogen storage disease type 1 is associated with poor metabolic control in type 1a and with granulocyte colony-stimulating factor therapy in type 1b DOI: 10.1159/000351022
2. Hepatic glycogen storage disorders: what have we learned in recent years? DOI: 10.1097/MCO.0000000000000181
3. Hypercalcemia in glycogen storage disease type I patients of Turkish origin. PMID: 22397040
4. Hyperlipidemia in glycogen storage disease type III: effect of age and metabolic control. DOI: 10.1007/s10545-008-0919-5
5. Glycogen storage disease type 1: impact of medium-chain triglycerides on metabolic control and growth. DOI: 10.1159/000283242
6. Glycogen storage disease type Ia: linkage of glucose, glycogen, lactic acid, triglyceride, and uric acid metabolism. DOI: 10.1016/j.jacl.2012.08.005
7. Urinary lactate excretion in type 1 glycogenosis--a marker of metabolic control or renal tubular dysfunction? PMID: 8739965
8. Prevention of complications in glycogen storage disease type Ia with optimization of metabolic control. DOI: 10.1111/pedi.12540
9. Serum concentrations of extracellular matrix components: novel markers of metabolic control and hepatic pathology in glycogen storage disease? PMID: 1919939
10. Clinical evaluation of a portable lactate meter in type I glycogen storage disease. DOI: 10.1007/s10545-005-0090-1
11. The activity of hepatic lipase and lipoprotein lipase in glycogen storage disease: evidence for a circulating inhibitor of postheparin lipolytic activity. DOI: 10.1203/00006450-198409000-00016
12. High Incidence of Serologic Markers of Inflammatory Bowel Disease in Asymptomatic Patients with Glycogen Storage Disease Type Ia. DOI: 10.1007/8904_2015_452
13. Clinical and biochemical heterogeneity between patients with glycogen storage disease type IA: the added value of CUSUM for metabolic control. DOI: 10.1007/s10545-017-0039-1
14. Continuous glucose monitoring in children with glycogen storage disease type I. Kasapkara ÇS, Cinasal Demir G, Hasanoğlu A, Tümer L. Eur J Clin Nutr. 2014 Jan;68(1):101-5. doi: 10.1038/ejcn.2013.186. Epub 2013 Oct 23. PMID: 24149443.
15. Continuous glucose monitoring in the treatment of obesity in patients with glycogen storage disease type Ia. Korljan Jelaska B, Ostojić SB, Berović N, Kokić V. Endocrinol

Diabetes Metab Case Rep. 2013;2013:130056. doi: 10.1530/EDM-13-0056. Epub 2013 Dec 1. PMID: 24683476

16. The use of continuous glucose monitoring in the practical management of glycogen storage disorders. White FJ, Jones SA. J Inherit Metab Dis. 2011 Jun;34(3):631-42. doi: 10.1007/s10545-011-9335-3. Epub 2011 May 10. PMID: 21556835
17. Continuous glucose monitoring in conditions other than diabetes. Maran A, Crepaldi C, Avogaro A, Catuogno S, Burlina A, Poscia A, Tiengo A. Diabetes Metab Res Rev. 2004 Nov-Dec;20 Suppl 2:S50-5. PMID: 15551341.
18. Continuous glucose monitoring in children with glycogen storage disease type I. Hershkovitz E, Rachmel A, Ben-Zaken H, Phillip M. J Inherit Metab Dis. 2001 Dec;24(8):863-9. PMID: 11916320.
19. A case of perioperative glucose control by using an artificial pancreas in a patient with glycogen storage disease. Yatabe T, Nakamura R, Kitagawa H, Munekage M, Hanazaki K. J Artif Organs. 2016 Mar;19(1):100-3. doi: 10.1007/s10047-015-0855-8. Epub 2015 Jul 21. PMID: 26194122
20. A preliminary study of telemedicine for patients with hepatic glycogen storage disease and their healthcare providers: from bedside to home site monitoring. Hoogeveen IJ, Peeks F, de Boer F, Lubout CMA, de Koning TJ, Te Boekhorst S, Zandvoort RJ, Burghard R, van Spronsen FJ, Derks TGJ. J Inherit Metab Dis. 2018 Mar 29. doi: 10.1007/s10545-018-0167-2. [Epub ahead of print] PMID: 29600495.
21. Role of continuous glucose monitoring in the management of glycogen storage disorders. Herbert M, et al. PMID: 29802555

Conclusion of articles:

1. Metabolic control is poorly defined. There is a urgent need for markers that are more relevant to the mechanisms leading to metabolic derangement and/or complications.

2. Metabolic control is directly affected by dietary management, age, and complications that occur.
3. The markers used for determining metabolic control are linked together.
4. Markers for metabolic control can be found in blood, urine, but also other areas such as the extracellular matrix should be examined.
5. New methods of measurements can be involved to define metabolic control in a home-setting, but also in a more continuous manner.
6. Continuous glucose monitoring has been used in liver GSD for prevention and monitoring of glycemia, perioperative care and for specific patient questions (such as first school day).
7. There is a suggestion of incorporating CGM data for big data analysis for a better understanding of the individual patient and metabolic control.
8. The CGMS was found to be a safe, effective, and reliable method for optimizing treatment in patients with GSD I, III, and IX.
9. There has been discussion in literature on the accuracy of CGM in comparison with other methods. This should be examined more systematically, especially for very low glucose levels.

Summary Question answered:

Partly. Literature is clear that metabolic control is poorly defined and that there is an urgent

need for markers for better detection. These are mostly opinions. Furthermore, there are studies that identify new ways of monitoring metabolic control. Therefore, I do propose that we adapt the question to: “What is the role for”**.**

Final Summary Question:

Changed:

What is the role for new methods for monitoring metabolic control (like noninvasive continuous glucose and lactate measurements, new biomarkers) for patients with liver Glycogen Storage Disease?

Code: G1Pre1

How can we improve counselling and management for pregnancy and lactation of patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“Pregnancy”[Mesh] OR “Pregnancy”[tiab] OR “Lactation”[Mesh] OR “Lactation”[tiab]).

Search Strategy Web of Science:
TOPIC: (glycogen storage disease) AND (TOPIC: (pregnancy) OR TOPIC: (lactation))

Search Strategy Embase:
'glycogen storage disease'/exp AND ('pregnancy'/exp OR 'lactation'/exp).

Found articles:
1. Title: Management of hepatic adenomatosis
Authors: Thapar M, et al.
Year of publication: 2015
PMID: 25740249

2. Title: Pregnancy in women with glycogen storage disease type Ia and Ib.
Authors: Ferrecchia IA, et al.
Year of publication: 2014.
PMID: 24476649

3. Title: Fertility and Pregnancy in women affected by glycogen storage disease type I, results of a multicenter Italian study.
Authors: Sechi A, et al.
Year of publication: 2013
PMID: 22562700

4. Title: Contraception and pregnancy in women affected by glycogen storage diseases
Authors: Mairovitz V, et al.
Year of publication: 2002
PMID: 12373581

Conclusion of articles:

1. During complications such as hepatic adenomatotis pregnancy is discouraged, but management is individualized.
2. Pregnancy in patients with GSD Ia and Ib poses challenges during gestation and delivery. Good metabolic control before conception and throughout pregnancy is

directly related to successful outcomes. But there is no nursing literature to date addressing perinatal and neonatal care in this population.

3. There can be a high prevalence of irregular menstruation cycles and polycystic ovaries, but fertility does not seem to be impaired. Monitoring for adenoma development is mandatory.
4. Contraception has to be adapted to the specific metabolic requirements of woman with GSD.
5. There may be selection bias in literature towards positive outcomes

Summary Question answered:
Partly. There are certain areas that are now not specified. We propose that we can add more focus on perinatal care.

Final Summary Question:

Changed:

How can we improve counselling and perinatal management (including lactation) for patients with liver Glycogen Storage Disease?

Code: G1Scr1
Is population neonatal screening possible for liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("Screening"[tiab] OR "Neonatal Screening"[mesh])

Found articles:

1. A novel image-based high-throughput screening assay discovers therapeutic candidates for adult polyglucosan body disease. DOI: 10.1042/BCJ20170469
2. A capillary electrophoresis procedure for the screening of oligosaccharidoses and related diseases. DOI: 10.1007/s00216-014-7832-6
3. Rapid molecular diagnosis of genetic diseases by high resolution melting analysis: fabry and glycogen storage 1A diseases. DOI: 10.1089/gtmb.2013.0371
4. Biochemical characteristics and increased tetraglucoside excretion in patients with phosphorylase kinase deficiency. DOI: 10.1007/s10545-005-0095-9
5. Fanconi-Bickel syndrome presenting in neonatal screening for galactosaemia. PMID: 9266402

Conclusion of articles:
In general there have not been formal studies into liver glycogen storage disease incorporation into (population or specified) newborn screening.

1. Screening for oligosaccharides, tetraglucoside and a-glucosidase have been proposed as possible screening markers.
2. GSD XI has been picked up in the screening for galactosemia.
3. There are populations in which there is NBS for GSD type II.

Summary Question answered:
No. I do propose that we put “population” between brackets to have options as specific new born screening for groups that are at risk open.

Final Summary Question:

Changed:

Is (population) neonatal screening possible for liver Glycogen Storage Disease?

Code: G1QoL1
How can we improve the quality of life of patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("quality of life"[mesh] OR "quality of life"[tiab])

Found articles:

1. Sleep and quality of life of patients with glycogen storage disease on standard and modified uncooked cornstarch. DOI: 10.1016/j.ymgme.2017.09.003
2. Safety and Efficacy of Chronic Extended Release Cornstarch Therapy for Glycogen Storage Disease Type I. DOI: 10.1007/8904_2015_488
3. Hepatic glycogen storage disorders: what have we learned in recent years? DOI: 10.1097/MCO.0000000000000181
4. Quality of life in adult patients with glycogen storage disease type I: results of a multicenter italian study. DOI: 10.1007/8904_2013_283
5. Psychosocial functioning in youth with glycogen storage disease type I. DOI: 10.1093/jpepsy/jsn017
6. Safety issues associated with dietary management in patients with hepatic glycogen storage disease. Steunenberg TAH, Peeks F, Hoogeveen IJ, Mitchell JJ, Mundy H, de Boer F, Lubout CMA, de Souza CF, Weinstein DA, Derks TGJ. Mol Genet Metab. 2018 Sep;125(1-2):79-85. doi: 10.1016/j.ymgme.2018.07.004. Epub 2018 Jul 18.

Conclusion of articles:
There have been several articles that demonstrate that quality of life can be reduced in liver GSD.

1. Quality of life seems to be affected as in other chronic diseases.
2. Strict dietary treatment, supplementation with probiotics and prevention of complications appears to increase quality of life.
3. The patient's perspective on the safety and quality of dietary management is important to take into account when answering this question.

Summary Question answered:
No. There are still many options that can be explored to improve the quality of life of liver GSD patients.

Final Summary Question:

The same

How can we improve the quality of life of patients with liver Glycogen Storage Disease?

Code: G1SH1
Should there be more information and research on synergistic heterozygosity / mixed liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("Heterozygosity"[tiab] OR "Mixed"[tiab])

Found articles:
None of relevance.

Conclusion of articles:
None.

Summary Question answered:
No. I propose we adapt the summary question

Final Summary Question:

The same:

Should there be more information and research on synergistic heterozygosity / mixed liver

Glycogen Storage Disease?

Code: G1Com1a
How to treat and/or prevent muscle problems in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh] OR “prevention”[tiab]) AND ("muscle problem*"[tiab] OR “muscle”[tiab])

Found articles:

1. Title: Diagnosis and management of glycogen storage disease type I: a practice guideline of the American College of Medical Genetics and Genomics, Authors: Kishnani PS, et al., Year of publication: 2014, doi:10.1038/gim.2014.128
2. Dietary management in glycogen storage disease type III: what is the evidence? Derks, TG, Smit GP, J Inherit Metab Dis. 2015 May;38(3):545-50. doi: 10.1007/s10545-014-9756-x. Epub 2014 Aug 28.

Conclusion of articles:
1. GSD I: a normal creatine phosphokinase concentration does not rule out muscle-related symptoms and signs
2. GSD III: A high protein diet may be beneficial in three ways: with gluconeogenesis intact, protein-derived alanine can be used as an alternate source for glucose during times of fasting; higher dietary protein intake may also improve muscle function by enhancing muscle protein synthesis; and by replacing some of the carbohydrates with protein, unnecessary glycogen storage may be reduced.
3. providing too much CS, too much formula, or excessively large meals can lead to excess glycogen storage in the liver and muscle and also to insulin resistance.
4. Physical therapy evaluation and intervention based on physical status and function
5. Coordination with a metabolic nutritionist regarding monitoring and optimizing blood glucose concentrations based on levels of exercise and activity
6. regular moderate aerobic exercise may be beneficial. Intense exercise should probably be avoided as it may promote rhabdomyolysis and muscle cramping.

Summary Question answered:
Partly, but especially there are unanswered questions regaring adult GSD IIIa patients. A high protein diet may be beneficial in GSD III. Too much CS/formula can lead to excess glycogen storage in the muscle. Further, regular moderate aerobic exercise may be beneficial. But these are only suggestions and more larger studies longitudinal are necessary to evaluate treatment and to investigate prevention programmes. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to prevent and/or treat muscle problems in patients with liver Glycogen Storage Disease?

Code: G1Com1b

How to treat and/or prevent heart problems in patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh] OR “prevention”[tiab]) AND ("heart problem*"[tiab] OR “heart”[tiab])

Found articles:

1. Title: Diagnosis and management of glycogen storage disease type I: a practice guideline of the American College of Medical Genetics and Genomics
Authors: Kishnani PS, et al.
Year of publication: 2014
doi:10.1038/gim.2014.128
2. Glycogen storage disease type III: diagnosis, genotype, management, clinical couse and outcome. Sentner CP, Hoogeveen IJ, Weinstein DA, Santer R, Murphy E, McKiernan PJ, Steuerwald U, Beauchamp NJ, Taybert J, Laforêt P, Petit FM, Hubert A, Labrune P, Smit GPA, Derks TGJ. J Inherit Metab Dis. 2016 Sep;39(5):697-704. doi: 10.1007/s10545-016-9932-2. Epub 2016 Apr 22.

Conclusion of articles:

1. Obtaining the tricuspid regurgitation jet by echocardiogram is the best method to periodically screen for elevated right-side heart pressures.
2. Echocardiography for ventricular hypertrophy including wall thickness, ventricular mass and systolic and diastolic function
o For GSD IIIa, obtain baseline and repeat every 12 – 24 months
For GSD IIIb, obtain baseline echocardiography for the same parameters as noted for GSD IIIa; repeat every 5 years
Routine 12-lead ECG for arrhythmia
o For GSD IIIa, serial 12-lead ECG every 2 years
o More detailed rhythm analysis if any symptoms
• Repeat echocardiograms and ECGs more frequently in patients with significant ventricular hypertrophy and/or clinical symptoms
3. For GSD Ia, there has been a lot of debate in literature on heart problems and cardiovascular problems. Alhough some case studies describe heart problems, there is no larger study showing an increased incidence of cardiovascular problems.

Summary Question answered:

Partly. In general the articles answer more monitoring of heart problems then treating/preventing. There is however no evidence for preventing heartproblems, mostly due to the lack of longitudinal data. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to prevent and/or treat heart problems in patients with liver Glycogen Storage Disease?

Code: G1Com1c

How to treat and/or prevent kidney problems in patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh] OR “prevention”[tiab]) AND ("kidney problem*"[tiab] OR “kidney”[tiab] OR “renal”[tiab])

Found articles:

1. Title: Diagnosis and management of glycogen storage disease type I: a practice guideline of the American College of Medical Genetics and Genomics
Authors: Kishnani PS, et al.
Year of publication: 2014
doi:10.1038/gim.2014.128
2. ESGSD I
3. GeneReviews type I
Tight metabolic control plus ACE inhibitor therapy improves GSD I nephropathy. Okechuku GO, Shoemaker LR, Dambska M, Brown LM, Mathew J, Weinstein DA. J Inherit Metab Dis. 2017 Sep;40(5):703-708. doi: 10.1007/s10545-017-0054-2. Epub 2017 Jun 13.
4. Prevention of complications in glycogen storage disease type Ia with optimization of metabolic control. Dambska M, Labrador EB, Kuo CL, Weinstein DA. Pediatr Diabetes. 2017 Aug;18(5):327-331. doi: 10.1111/pedi.12540. Epub 2017 Jun 1.

Conclusion of articles:

1. Oral citrate supplementation will augment citrate excretion, favorably altering the urinary milieu to decrease the chances of urinary calcium precipitation and, as a result, is likely very beneficial in GSD I patients with low urinary citrate levels. Especially in GSD I individuals with known urinary tract calcification and ongoing hypercalciuria, thiazide diuretic therapy can be considered.
2. Haemodialysis, continuous ambulatory peritoneal dialysis and renal transplantation are all therapeutic options for end-stage renal disease in GSD I.
3. Angiotensin-converting enzyme (ACE) inhibitors such as captopril are used to treat microalbuminuria, an early indicator of renal dysfunction.
4. There are suggestions that tight metabolic control improves/prevents complications in liver GSD patients

Summary Question answered:

Partly. For GSD type I it is described how to treat and there are also some studies on prevention. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to prevent and/or treat kidney problems in patients with liver Glycogen Storage Disease?

Code: G1Com1d
How to treat and/or prevent intestinal problems in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh] OR “prevention”[tiab]) AND (“intestines”[Mesh] OR "intestinal problem*"[tiab] OR “intestinal”[tiab] OR “abdominal”[tiab])

Found articles:
1. Title: Inflammatory bowel disease in glycogen storage disease type Ib
Authors: Roe TF, et al. Year of publication: 1986 doi: 10.1016/S0022-3476(86)80572-8.
2. Title: Brief Report: Treatment of Chronic Inflammatory Bowel Disease in Glycogen Storage Disease Type Ib with Colony-Stimulating Factors. Authors: Roe TF, et al. Year of publication: 1992. DOI: 10.1056/NEJM199206183262504
3. Title: Long term G-CSF-induced remission of ulcerative colitis-like inflammatory bowel disease in a patient with glycogen storage disease Ib and evaluation of associated neutrophil function. Authors: Alsultan A, et al. Year of publication: 2010. PMID: 20830779
4. Title: Granulocyte colony-stimulating factor in glycogen storage disease type 1b. Results of the European Study on Glycogen Storage Disease Type 1. Authors: Visser G, et al. PMID: 12373578
5. Inflammatory Bowel Disease in Glycogen Storage Disease type Ia. Lawrence NT1, Chengsupanimit T, Brown LM, Derks TG, Smit GP, Weinstein DA. J Pediatr Gastroenterol Nutr. 2017 Feb;64(2):e52-e54. doi: 10.1097/MPG.0000000000000592.
6. Neutropenia in glycogen storage disease Ib: outcomes for patients treated with granulocyte colony-stimulating factor. Dale DC, Bolyard AA, Marrero T, Kelley ML, Makaryan V, Tran E, Leung J, Boxer LA, Kishnani PS, Austin S, Wanner C, Ferrecchia IA, Khalaf D, Maze D, Kurtzberg J, Zeidler C, Welte K, Weinstein DA. Curr Opin Hematol. 2019 Jan;26(1):16-21. doi: 10.1097/MOH.0000000000000474.

Conclusion of articles:
IBD is associated with GSD type Ib, and leukopenia/neutropenia may play a role in the pathogenesis of intestinal inflammation. This assumption is supported by evidence that colony stimulating factors can improve IBD-like disease in patients with GSD type Ib. There are some case studies that describe IBD-like disease to GSD Ia.

Summary Question answered:
Partly. However, treatment is not optimal and has many side-effects. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to better prevent and/or treat intestinal problems in patients with liver Glycogen Storage Disease?

Code: G1Com1e
How to treat and/or prevent liver problems in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh] OR “prevention”[tiab]) AND ("liver problem*"[tiab] OR “liver”[tiab] OR “hepatic”[tiab] OR “hepatic problem*”[tiab])

Found articles:
1. Title: Hepatic glycogen storage disorders: what have we learned in recent years?
Authors: Burda P, et al.
Year of publication: 2015
DOI: 10.1097/MCO.0000000000000181
2. ACMG guidelines
3. EGSDI
4. Genereviews
5. Glycogen storage disease type Ia: adult presentation with microcytic anemia and liver adenomas. Moest W, van der Deure W, Koster T, Spee-Dropková M, Swart-Busscher L, de Haas RJ, Derks TGJ. Hepatology. 2018 Aug;68(2):780-782. doi: 10.1002/hep.29858. Epub 2018 Apr 27.

Conclusion of articles:
1. GSD I Development of liver adenomas is frequent, with a risk of rupture and bleeding, local compression, and progression into malignancy (hepatocellular carcinoma). Evidence is accumulating that poor ‘metabolic control’ may be a risk factor for adenoma formation. High triglyceride levels are negatively correlated with adenoma-free survival. In line with this observation, regression of adenoma size was documented in some patients once better metabolic control with lower triglycerides was achieved. However, liver adenomas can also develop in patients with good and stable metabolic control, and the biology of adenoma formation in GSD I still is incompletely understood.
2. Recurrent hypoglycemia causes lactic acidosis, hepatomegaly, hypertriglyceridemia, hyperuricemia, and failure to thrive in the young child. Thus, avoidance of fasting is the first line of treatment in GSD I. To prevent hypoglycemia, small frequent feedings high in complex carbohydrates (preferably those higher in fiber) are evenly distributed over 24 hours.
3. The cause for HCC is unclear, but there appears to be an adenoma-to-HCC transformation, rather than HCC arising in normal or cirrhotic liver tissue. There is no effective biomarker because α-fetoprotein and carcinoembryonic antigen levels are often normal even in the setting of HCC. No good imaging tool separates HCA from HCC.
4. Currently, there is no biomarker that is predictive of HCC transformation in GSD III. Alpha fetoprotein and chorionic embryonic antigen levels may remain normal and lack sensitivity predicting the presence of hepatocellular adenomas or malignant transformation
5. Liver transplantation may be indicated, for instance for those with severe hepatic cirrhosis, liver dysfunction, and/or hepatocellular carcinoma.
6. In some instances there are even patients that present in adulthood, that already have complications.

Summary Question answered:
Partly. Till now the only recommendation is to have a good ‘metabolic control’, for which

there is good evidence that this treats liveradenomas. Besides, liveradenomas can be treated surgically (ablation, coiling, liver transplantation). But there is much that needs to be cleared up on fibrosis and the pathophysiology. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to prevent and/or treat liver problems in patients with liver Glycogen Storage Disease?

Code: G1Com1f
How to treat and/or prevent oncological problems (i.e. Leukemia) in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh] OR “prevention”[tiab]) AND ("neoplasms”[Mesh] OR “oncological problem*”[tiab] OR “cancer”[tiab] OR “leukemia”[tiab])

Found articles:
1. ACMG
2. Genereviews GSD I
3. A Third Case of **Glycogen Storage Disease** IB and Giant Cell Tumour of the Mandible: A Disease Association or Iatrogenic Complication of Therapy.
Prasad R, Estrella J, Christodoulou J, McKellar G, Tchan MC.
JIMD Rep. 2018;42:5-8. doi: 10.1007/8904_2017_67. Epub 2017 Nov 9.
PMID: 29119402

4. Gastric cancer following a **liver transplantation** for **glycogen storage disease** type Ia (von Gierke disease): A case report.
Xiao H, Bian J, Zhang L, Wang Z, Ding A.
Oncol Lett. 2014 Dec;8(6):2803-2805. Epub 2014 Oct 9.
PMID:25364469
5. Neutropenia in glycogen storage disease Ib: outcomes for patients treated with granulocyte colony-stimulating factor. Dale DC, Bolyard AA, Marrero T, Kelley ML, Makaryan V, Tran E, Leung J, Boxer LA, Kishnani PS, Austin S, Wanner C, Ferrecchia IA, Khalaf D, Maze D, Kurtzberg J, Zeidler C, Welte K, Weinstein DA. Curr Opin Hematol. 2019 Jan;26(1):16-21. doi: 10.1097/MOH.0000000000000474.

Conclusion of articles:
1. Tthe risk of acute myelogenous leukemia is very low. However, all patients should be observed, with serial blood counts monitored approximately quarterly for development of loss of response to G-CSF, presence of myeloblasts in the blood, evidence of hypersplenism, new patterns of bone pain, or any other changes that might suggest a change in hematological disease or development of a myeloid malignancy. Besides this, certain other types of cancer have been described in case reports.

Summary Question answered:
No. Additional data in larger cohorts is necessary to answer the question. No specific treatment of prevention of oncological problems mentioned in articles. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to prevent and/or treat oncological problems (i.e. Leukemia) in patients with liver Glycogen Stoage Disease?

Code: G1Com1g

How to treat and/or prevent immunological problems (i.e. Infections) in patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh] OR “prevention”[tiab]) AND ("infection”[Mesh] OR “immunological problem*”[tiab] OR “infection*”[tiab])

Found articles:

1. Title: Congenital neutropenia: diagnosis, molecular bases and patient management
Authors: Donadieu J, Et al.
Year of publication: 2011
PMID: 21595885
2.Title: Vitamin E supplementation improves neutropenia and reduces the frequency of infections in patients with glycogen storage disease type 1b.
Authors: Melis D, et al.
Year of publication: 2009
PMID: 19066956
3. Neutropenia in glycogen storage disease type Ib: outcomes for patients treated with granulocyte colony-stimulating factor, Dale DC et al, Curr Opin Hematol. 2019 Jan;26(1):16-21. PMID: 30451720

Conclusion of articles:

1. GSD Ib: This susceptibility to infections is due to neutropenia and, sometimes, to neutrophil dysfunction (mainly defective chemotactism). Bone marrow smears show hyperplasia of the granulocytic lineage, without maturation arrest (Additional file 1, Figure S1 Plate #7). The origin of the neutropenia and neutrophil dysfunction is not known. It is not related to nutritional status and is not corrected by liver transplantation [68]. This, and the lack of any known role of the Gluco 6 Phosphate translocase (gene SLC37A4, previously named G6PT1), in neutrophil energy metabolism, raises the possibility that this protein has another function in neutrophils. Gene therapy in a mouse model has corrected both the metabolic and myeloid disorders
2. GSD Ib: The use of vitamin E and its effectiveness in reducing the frequency of infection and improving neutropenia has been reported.
3. GSD I: As a result, individuals with low urinary citrate levels are more pre- disposed to urinary tract calcifications, and such urinary tract calcifications can increase the chances of urinary tract infection or mediate renal parenchymal damage with loss of renal functional reserve.
4. G-CSF has been used for treating neutropenia and preventing infections in patients with GSD Ib since 1989
5. Routine immunizations should be scheduled as recommended by the Centers for Disease Control and Prevention (http://www.cdc.gov/vaccines/schedules/). Other available immunizations, such as those for seasonal influenza, hepatitis B, and pneumococcal infections (polyvalent after 2 years of age), should be offered because they can prevent the hypoglycemia caused by the gastrointestinal manifestations associated with the disease processes.
6. Routine immunizations should be given on the recommended schedule for GSD IX

Summary Question answered:
Partly. There are many articles on preventing infections. Furthermore, there are some case reports that describe auto-immune disease. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to prevent and/or treat immunological problems (i.e. Infections) in patients with liver Glycogen Storage Disease?

Code: G1Com1h

How to treat and/or prevent hormonal problems (i.e. thyroid, menstrual cycle, growth, diabetes, insulin response) in patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh] OR “prevention”[tiab]) AND (“hormonal problems”[tiab] OR “thyroid*”[tiab] OR “menstrual*”[tiab] OR "growth”[tiab] OR “diabetes*”[tiab] OR “insuline*”[tiab])

Found articles:

1. Title: Hypogonadotropic Hypogonadism in Males with Glycogen Storage Disease Type 1. Authors: Wong EM, et al. Year of publication: 2017 PMID: 28160246

2. ACMG

3. Oki Y, Okubo M, Tanaka S, Nakanishi K, Kobayashi T, Murase T. Diabetes mellitus secondary to glycogen storage disease type III. *Diabet Med* 2000;17:810 – 812.

4. IGSDIII

5. Lee PJ, Patel A, Hindmarsh PC, Mowat AP, Leonard JV. The prevalence of polycystic ovaries in the hepatic glycogen storage diseases: its association with hyperinsulinism. Clin Endocrinol (Oxf) 1995;42:601–606.

6. Insulin-resistance in glycogen storage disease type Ia: linking carbohydrates and mitochondria, Rossi A, et al, J Inherit Metab Dis, 2018 Nov;41(6):985-995. DOI: 10.1007/s10545-018-0149-4

7. Glycogen storage disease type Ia (GSD Ia) but not Glycogen Storage Disease type Ib (GSD Ib) is associated to an increased risk of metabolic syndrome: possible role of microsomal glucose 6-phosphate accumulation, Melis D et al, Orphanet J Rare Dis. 2015 Jul 29;10:91. Doi: 10.1186/s13023-015-0301-2.

8. The growth hormone-insulin-like growth factor axis in glycogen storage disease type 1: evidence of different growth patterns and insulin-like growth factor levels in patients with glycogen storage disease type 1a and 1b. Melis D, et al. J Pediatr. 2010 Apr;156(4):663-70.e1. doi: 10.1016/j.jpeds.2009.10.032. Epub 2009 Dec 21.

Conclusion of articles:

1**. There is an association between** suboptimal metabolic control of GSD and hypogonadotropic hypogonadism

2. The risk of adenomas in GSD I patients, estrogen-based contraceptives should be avoided when possible.

3. However, normal growth can occur, provided that patients maintain good metabolic control at an early age.

4. Other complications of overfeeding, including increased glycogen storage, over time can lead to hyperinsulinemia and insulin resistance.

5. Insulin and insulin secretagogues (sulfonylureas) should be used with caution. Growth hormone treatment should also be avoided because it can result in the development or an increase in the size or number of liver adenomas, along with severe hyperlipidemia

6. Diabetes mellitus associated with liver cirrhosis is usually treated with insulin. However, administration of insulin to patients with GSD III carries a high risk, because glycogen degradation and glucose release by the liver is severely impaired in these patients. Kihara et al. reported that diabetes mellitus associated with chronic liver disease can be successfully treated with a newly developed hypoglycaemic agent, an alpha-glucosidase inhibitor. This drug is beneficial for the treatment of diabetes mellitus secondary to GSD III, because it blunts the post-prandial elevation of serum glucose levels by delaying the hydrolysis of carbohydrates in the intestinal tract, and there is little risk of inducing hypoglycaemia. Our patient was treated with the alpha-glucosidaseinhibitor voglibose with no adverse effects.
7. A polycystic ovarian appearance is a common finding In patients with glycogen storage disease even before puberty. In GSD-III and adults with GSD-la, this ovarian appearance was associated with hyperinsulinism, suggesting an aetiological link, but this was not the case in pre-pubertal children with GSD-la. Inborn errors of carbohydrate metabolism may act as useful models for examining control mechanisms of ovarian physiology and development.

Summary Question answered:
Partly. Several hormonal problems are mentioned with respect to treatment and prevention. Again, larger cohorts are lacking. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to prevent and/or treat hormonal problems (i.e. thyroid, menstrual cycle, growth, diabetes, insulin response) in patients with liver Glycogen Storage Disease?

Code: G1Com1i
How to treat and/or prevent neurological problems in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh] OR “prevention”[tiab]) AND (“neurological problems”[tiab] OR “neuro*”[tiab] OR “brain*”[tiab] OR “cerebral”[tiab])

Found articles:
1. EGSDI

Conclusion of articles:
1. By adjusting metabolic control in GSD I patients as optimal as possible, the occurrence of symptoms/complications directly related to metabolic disturbances will diminish: growth improves, liver size decreases, the risk of gout, urolithiasis, xanthomas and pancreatitis decreases, platelet function normalises, and, as long as cerebral symptoms (coma, convulsions) of acute metabolic decompensation can be prevented, cerebral function is preserved.
2. Certain subtypes of GSD IV have also been described with severe neurological dysfunction. There is little in literature on treatment or prevention.
3. GSD III has been described to have relative cognitive dysfunction in specific tests. Treatment and prevention is not mentioned.

Summary Question answered:
No. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to prevent and/or treat neurological problems in patients with liver Glycogen Storage Disease?

Code: G1Com1j
How to treat and/or prevent hematological problems (i.e. anemia) in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh] OR “prevention”[tiab]) AND (“hematological problems”[tiab] OR “hematological*”[tiab] OR “anemia*”[tiab])

Found articles:
1. ACMG
2. Neutropenia in glycogen storage disease type Ib: outcomes for patients treated with granulocyte colony-stimulating factor, Dale DC et al, Curr Opin Hematol. 2019 Jan;26(1):16-21. PMID: 30451720

Conclusion of articles:
1. If iron deficiency anemia is documented, iron supplementation (oral or i.v.) as needed and optimization of metabolic control are recommended. Consider iron refractory anemia (in GSd Ia associated with adenomas and in GSD Ib with IBD) if iron levels do not improve.
2. Standard management of patients with platelet dysfunction/ von Willebrand disease include antifibrinolytics and deamino-8-d-arginine vasopressin, which acts by stimulating factor VIII from endothelial cells and improving von Willebrand factor activity and the platelet release reaction. These agents could be utilized in patients with GSD I when clinically indicated, but use of deamino-8-d-arginine vasopressin in GSD I must be performed with caution because of the risk of fluid overload and hyponatremia in the setting of i.v. glucose administration

Summary Question answered:
Partly. Treatment methods are mentioned, but not with respect to larger cohorts. Prevention is not mentioned. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to prevent and/or treat hematological problems (i.e. anemia) in patients with liver Glycogen Storage Disease?

Code: G1Com1k
How to treat and/or prevent dental problems in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh] OR “prevention”[tiab]) AND (“dental problems”[tiab] OR “dental”[tiab] OR “oral manif*”[tiab])

Found articles:
1. Title: Unusual Oral Manifestations and Evolution in Glycogen Storage Disease Type Ib
Authors: Mortallaro CDMD, et al.
Year of publication: 2006
ISSN: 1049-2275
2. ACMG

Conclusion of articles:
1. GSD IB: Common intraoral manifestations are dental caries, gingivitis, periodontal disease, delayed dental maturation and eruption, oral bleeding diathesis, and oral ulcers.
2. GSD IB: Good dental hygiene and frequent monitoring of dental health are advised. Antibiotic coverage is not needed for routine dental cleaning, but it is indicated in the case of gingivitis or in case of oral infections with risk for cellulitis/sepsis due to neutropenia.

Summary Question answered:
Partly. Some methods of treatment and prevention are mentioned, but it still occurs a lot. For GSD IB dental hygiene and frequent monitoring of dental health is advised. Antibiotic coverage is not needed for routine dental cleaning, but it is indicated in the case of gingivitis or in case of oral infections with risk for cellulitis/sepsis due to neutropenia. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to prevent and/or treat dental problems in patients with liver Glycogen Storage

Disease?

Code: G1Com1l

How to treat and/or prevent psychiatric problems in patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh]) AND (“psychiatric problems”[tiab] OR “psychiatry*”[tiab] OR “psychological”[tiab] OR “psychologi*”[tiab])

Found articles:
1. Title: Cognitive profile of patients with glycogen storage disease type III: a clinical description of seven cases.
Authors: Michon CC, et al.
Year of publication: 2015
PMID: 25388549
2. IGSDIII

Conclusion of articles:

1. GSD III: The impairment in social cognition (recognition of emotions and ability to attribute mental states to others) and executive functions observed could be a consequence of orbito-frontal dysfunction due to the abnormal glycogen metabolism characteristic of the underlying disease. These results are consistent with the hypothesis of a central nervous system involvement in patients with GSDIII, but need to be confirmed in future research.
2. In general, overtreating can also lead to excess weight gain, which negatively impacts the child in many ways, both psychologically and medically.
3. As with all metabolic disorders, other important issues related to feeding should not be overlooked. These include psy- chosocial issues and exercise. All children have a need for structure and guidance with their diet, but this is especially true for children with special diets. Early establishment of healthy dietary habits consistent with GSD III guidelines will improve the likelihood of long-term dietary compliance. Teaching chil- dren about their GSD III diet and its importance in ways that are age appropriate will help them gain independence and take ownership of their dietary needs as they grow older. When consistently providing this structure, it is also important to maintain as much normalcy about the diet as possible, so that the child does not feel isolated or adopt a negative view of the diet. Choices within the framework of the diet will allow the children to feel that they have some control. Offering more choices in other areas of their life will also give the child a sense of control.

Summary Question answered:

No. As discussed in the G2Depr1 question, we propose to add these question together and add “i.e. depression” to not lose this important bit of information. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

How to prevent and/or treat psychiatric problems (i.e. depression) in patients with liver Glycogen Storage Disease?

Code: G1Com1m

How to treat and/or prevent hyperlipidemia and in patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh]) AND (“hyperlipidemias”[Mesh] OR “hyperlipidemia”[tiab] OR “dyslipidemia*”[tiab] OR “hyperlipd*”[tiab] OR “dyslipid*”[tiab])

Found articles:

1. Title: Secondary Hypertriglyceridemia
Authors: Blackett PR, et al.
Year of publication: 2016
PMID: 27809435
2. Title: Increased de novo lipogenesis and delayed conversion of large VLDL into intermediate density lipoprotein particles contribute to hyperlipidaemia in GSD Ia
Authors: Bandsma RHJ
Year of publication: 2008
PMID: 18520334
3. Lipids in hepatic glycogen storage diseases: pathophysiology, monitoring of dietary management and future directions. Derks TG, et al. J Inherit Metab Dis. 2015 May;38(3):537-43. Doi: 10.1007/s10545-015-9811-2

Conclusion of articles:

1. However, to effectively normalize the TG, frequent corn-starch dosing is needed to achieve blood glucose levels continuously above 75 mg/dL, especially at night.(95) This approach involves high carbohydrate intakes, which in the long term may increase VLDL production often resulting in requirement for lipid lowering medications.(96)
2. GSD Ia: Fibrates decrease plasma triglyceride concentrations. Use of statins lower cholesterol synthesis rates would likely have a strong effect on plasma cholesterol levels, although currently no data available.
3. Although effects of hyperlipidemia in GSD I have been studied for decades, there is no consensus regarding the long-term complications or the best treatment for hyperlip- idemia in this disorder. Both dietary and pharmacological treat- ments have been studied, including fibrates, statins, niacin, and fish oil. The effect of medium-chain triglycerides on lowering cholesterol and triglycerides is currently being studied.[1]The use of vitamin E and its effectiveness in reducing the frequency of infection and improving neutropenia has been reported.
4. Management of hyperlipidemia with medications usually does not begin until the patient is at least 10 years old
5. Hyperlipidemia in GSD Ia can be managed with lipid-lowering drugs such as 3-hydroxy-3-methyl-glutaryl-CoA reductase inhibitors and fibrates. The potential benefit of 3-hydroxy- 3-methyl-glutaryl-CoA reductase inhibitors was emphasized by a study that showed increased triglyceride synthesis in GSD Ia patients compared with normal controls. But no consensus regarding the recommendation of lipid-lowering drugs has been reached.

6. GSD I: lipid-lowering medications for elevated lipid levels despite good metabolic control such as HMG-CoA reductase inhibitors and fibrate
7. GSD III: hormonal contraceptives and statins for control of hyperlipidemia.

Summary Question answered:
In the literature hyperlipidemia and hypertriglyceridemia is described and how to treat in GSD I and III. There is not much focus on prevention. Furthermore, there are many cases in which hyperlipidemia cannot be treated completely. I propose that we add “and its complication” to also further elaborate on the complications associated with hyperlipidemia. Addition from Terry to change the word ordering treat and/or prevent

Final Summary Question:

Changed

How to prevent and/or treat hyperlipidemia and its complications in patients with liver Glycogen Storage Disease?

Code: G1Com1n
How to treat and/or prevent overweight in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“therapeutics”[Mesh] OR “treatment”[tiab] OR “management”[tiab] OR “prevention and control”[Mesh]) AND (“overweight”[Mesh] OR “overweight”[tiab] OR “obese*”[tiab])

Found articles:
Same as G4Weight1.

Conclusion of articles:
Same as G4Weight1. I propose to merge this question with the question G4Weight1.

Summary Question answered:
-

Final Summary Question:

None.

Summary Questions Group 2

Code: G2Ost1
What is the proper management of osteoporosis in patients with Glycogen Storage Disease Type Ia?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("Osteoporosis"[Mesh] OR “osteoporosis”[tiab]) AND ("Disease Management"[Mesh] OR “management”[tiab])

Found articles:
1. Title: Prevention of complications in glycogen storage disease type Ia with optimization of metabolic control. Authors: Dambska M, et al. Year of publication: 2017. PMID: 28568353

2. ACMG guidelines

Conclusion of articles:
1. Calcium and vitamin D supplements to support bone growth and mineralization. If the individual is not on calcium-fortified soy milk, calcium citrate or calcium carbonate with vitamin D is recommended to meet RDA for age needs and to prevent nutritional deficiencies.

2. 25(OH)-vitamin D levels should be monitored routinely and treated as needed

3. DEXA scans are used to monitor bone density, but especially for the younger patients there is a lack of good reference values.

4. Good metabolic control appears to prevent the occurrence of osteoporosis.

Summary Question answered:
Partly. Till now it is monitoring with DEXA scan and monitor 25(OH)-vitamin D levels. Further is a good metabolic control important and calcium and vitamin D supplements. I propose to alter the question from “proper” to “optimal” management to note that there is already a management strategy, but that this strategy can be improved upon. Since osteoporosis is also mentioned in GSD Ib and GSD III, I propose to leave out the “Ia” to include all types. Furthermore, I would specify that this is not only about osteoporosis, but reduced bone mineral density and its complications, mentioning osteoporosis as an example, but also osteopenia or fractures can be included.

Final Summary Question:

Changed

What is the optimal management of reduced bone mineral density and its complications (i.e. osteoporosis) in patients with liver Glycogen Storage Disease?

Code: G2DD1
Can liver Glycogen Storage Disease cause developmental delays throughout childhood?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“developmental delay”[tiab])

Found articles:
1. ACMG guidelines

2. IGSDIII

3. Genereviews GSD VI

Conclusion of articles:
1. Cognitive development is usually normal unless the patient has cerebral damage from recurrent hypoglycemic episodes.

2. Early diagnosis reduces the risk of prolonged hypoglycemia, which, untreated, may cause developmental and physical delay, seizures with or without cerebral damage, and even death.

3. GSD III: subtle motor delay in children may be more widespread than previously identified, and a recent report described that 80% of children with GSD IIIa had average gross motor function below the 25th percentile for age.

4. Developmental delay, particularly for the motor milestones, may occur in untreated children. Intellectual development is normal in most children.

Summary Question answered:
Partly. In GSD I with good metabolic control the development is normal. In GSD III there is a subtle motor delay. This is not known for the other GSD types. The data is mostly based on cross-sectional measurements and not longitudinal data.

Final Summary Question:

The same:

Can liver Glycogen Storage Disease cause developmental delays throughout childhood?

Code: G2GD1
With proper treatment, are growth delays in liver Glycogen Storage Disease inevitable?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“growth delay”[tiab])

Found articles:
1. ACMG guidelines

2. IGSD III

3. Genereviews GSD I, III, VI

Conclusion of articles:
1. GSD I: Normal growth can occur, provided that patients maintain good metabolic control at an early age

2. GSD III: The child with myopathy and growth failure should be started on a high protein diet.

3. Short stature. Children with GSDI have poor growth and short stature in adulthood; however, with strict dietary regimens and control, growth and final adult stature have improved

4. GSD III: Growth may be compromised by poor metabolic control. Catch-up growth may be observed with the establishment of good metabolic control.

5. GSD VI: Some individuals with glycogen storage disease type VI (GSD VI) may not require any treatment, but most have better growth and stamina with therapy.

Summary Question answered:
Partly. There are many different findings in literature on the growth in liver GSD, some have growth delay, some not. Despite treatment, some patients experience growth delays. I propose to alter the question to how we can optimize treatment to prevent growth delays.

Final Summary Question:

Changed:

How can we optimize treatment to prevent growth delays in liver Glycogen Storage Disease?

Code: G2LE1
What is the life expectancy of patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“Life expectancy”[Mesh] OR “Life expectancy”[tiab])

Found articles:
None of relevance.

Conclusion of articles:
1. Many studies state that life-expectancy has improved considerable since the introduction of dietary treatment, but no statistics are mentioned. This is also a difficult question since there could be a bias that the patients who are now older, could also be afflicted with a relatively mild disease. Epidemiological studies and longitudinal cohort studies that take into account this bias could further the research in this field.

Summary Question answered:
No.

Final Summary Question:

The same:

What is the life expectancy of patients with liver Glycogen Storage Disease?

Merge between: G2IBD1 & G2Neu2 & G2Inf1
What is the mechanism behind neutropenia and Inflammatory Bowel Disease (IBD) in Glycogen Storage Disease Type Ib and can they be cured with gene therapy or a liver transplant?

G2IBD1:
When liver Glycogen Storage Disease is "cured" will there still be neutropenia and Inflammatory Bowel Disease (IBD) in Glycogen Storage Disease Ib?

G2Neu2:
What is the relationship between neutropenia and Inflammatory Bowel Disease (IBD) in Glycogen Storage Disease Type Ib?

G2Inf1
What causes inflammation in Glycogen Storage Disease Type Ia?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“Neutropenia”[tiab]) AND (“Inflammatory Bowel Disease”[tiab])

Found articles:

1. Survival, but not maturation, is affected in neutrophil progenitors from GSD-1b patients. **Visser G**1, **de Jager W**, **Verhagen LP**, **Smit GP**, **Wijburg FA**, **Prakken BJ**, **Coffer PJ**, **Buitenhuis M**. PMID:21863279; DOI: **10.1007/s10545-011-9379-4**

2. Antibodies to CBir1 are associated with glycogen storage disease type Ib. Davis MK[1], Valentine JF, Weinstein DA, Polyak S. PMID: 20410847. DOI: 10.1097/MPG.0b013e3181c15f78

3. A patient with common glycogen storage disease type Ib mutations without neutropenia or neutrophil dysfunction. Martens DH1, Kuijpers TW, Maianski NA, Rake JP, Smit GP, Visser G. PMID: 16601899 DOI: 10.1007/s10545-006-0146-x

4. Association of glycogen storage disease 1b and Crohn disease: results of a North American survey. Dieckgraefe BK1, Korzenik JR, Husain A, Dieruf L. PMID: 12373579 DOI: 10.1007/s00431-002-1011-z

5. Genotype/phenotype correlation in glycogen storage disease type 1b: a multicentre study and review of the literature. Melis D1, Fulceri R, Parenti G, Marcolongo P, Gatti R, Parini R, Riva E, Della Casa R, Zammarchi E, Andria G, Benedetti A. PMID: 15906092 DOI: 10.1007/s00431-005-1657-4

6. Inflammatory bowel disease in glycogen storage disease type Ib.

Roe TF, Thomas DW, Gilsanz V, Isaacs H Jr, Atkinson JB. Inflammatory bowel disease in glycogen storage disease type Ib.

Conclusion of articles:

1. Older studies already show that inflammatory bowel disease appears to be associated with GSD Ib and neutrophile abnormalities may be involved in the pathogenesis of bowel inflammation.
2. There is a strong association between GSD Ib and Inflammatory bowel disease which was shown in an North American survey. They hypothesise that some forms of inflammatory bowel disease may result from impaired mucosal innate immunity.
3. Survival of neutrophile progenitors is affected in GSD Ib patients, and maturation is not.
4. Antibodies that are associated with Crohne-like colitis are present in most GSD Ib patients.
5. There have been case reports of GSD Ib patients that have no neutrophil disfunction, infections or inflammatory bowel disease.
6. As of yet, no genotype/phenotype relation has been established for GSD Ib and neutrophile disfunction, infections or inflammatory bowel disease.

Summary Question answered:

No, although there are some hypotheses in literature on the mechanism between GSD Ib, neutropenia and IBD, there is no concrete evidence. I would propose to drop the examples of gene therapy or liver transplantation to also include more examples (bone marrow transplant) or other types of treatment, and also to shorten the question.

Final summary question:

Changed:

What is the mechanism behind neutropenia and Inflammatory Bowel Disease (IBD) in Glycogen Storage Disease Type Ib and can these complications be cured?

Merge between: G2Neu1 & G2Neu3 & G2Neu4 & G2Bone1
What is the best therapy for neutropenia and infections (G-CSF or alternatives) considering outcomes, complications and side effects (i.e. bone pain) in patients with Glycogen Storage Disease Type Ib (or Ia)?

G2Neu1:
How do you improve neutropenia and prevent infections in Glycogen Storage Disease Type Ib (and Ia)?

G2Neu3:
How does neupogen dosing affect outcomes and complications in patients with Glycogen Storage Disease Type Ib?

G2Neu4:
Are there other therapies for neutropenia than G-CSF for patients with Glycogen Storage Disease Type Ib?

G2Bone1:
Can bone pain be avoided when using G-CSF in Glycogen Storage Disease Type Ib?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“Neutropenia”[tiab])

Found articles:

1. Neutropenia in glycogen storage disease Ib: outcomes for patients treated with granulocyte colony-stimulating factor. Dale DC, Bolyard AA, Marrero T, Kelley ML, Makaryan V, Tran E, Leung J, Boxer LA, Kishnani PS, Austin S, Wanner C, Ferrecchia IA, Khalaf D, Maze D, Kurtzberg J, Zeidler C, Welte K, Weinstein DA. PMID: 30451720 DOI: 10.1097/MOH.0000000000000474
2. Vitamin E Improves Clinical Outcome of Patients Affected by Glycogen Storage Disease Type Ib. Melis D, Minopoli G, Balivo F, Marcolongo P, Parini R, Paci S, Dionisi-Vici C, Della Casa R, Benedetti A, Andria G, Parenti G. PMID: 26122627. DOI: 10.1007/8904_2015_461

3. Prolonged granulocyte colony stimulating factor use in glycogen storage disease type 1b associated with acute myeloid leukemia and with shortened telomere length.
Li AM, Thyagu S, Maze D, Schreiber R, Sirrs S, Stockler-Ipsiroglu S, Sutherland H, Vercauteren S, Schultz KR.
Pediatr Hematol Oncol. 2018 Feb;35(1):45-51. doi: 10.1080/08880018.2018.1440675. Epub 2018 Apr 13.
PMID: 29652549

4. Matched unrelated donor transplantation in glycogen storage disease type 1b patient corrects severe neutropenia and recurrent infections. Mehyar LS, Abu-Arja R, Rangarajan HG, Pai V, Bartholomew DW, Rose MJ, Bajwa RPS. PMID: 29515247 DOI: 10.1038/s41409-018-0147-z

5. Bone marrow transplantation in glycogen storage disease type 1b. Pierre G1, Chakupurakal G, McKiernan P, Hendriksz C, Lawson S, Chakrapani A. PMID: 18206704 DOI: 10.1016/j.jpeds.2007.09.031

6. Granulocyte colony-stimulating factor in glycogen storage disease type 1b. Results of the European Study on Glycogen Storage Disease Type 1. Visser G1, Rake JP, Labrune P, Leonard JV, Moses S, Ullrich K, Wendel U, Groenier KH, Smit GP. PMID: 12373578 DOI: 10.1007/s00431-002-1010-0

Conclusion of articles:

1. G-CSF is effective to raise blood neutrophil counts and reduce fevers and infections in most patients. In conjunction with other therapies (salicylates, mesalamine sulfasalazine and prednisone), G-CSF ameliorates inflammatory bowel symptoms, but doses must be limited because it increases spleen size associated with abdominal pain

2. Vitamin E Improves Clinical Outcome of Patients Affected by Glycogen Storage Disease Type Ib
3. Matched unrelated donor bone marrow transplantation in glycogen storage disease type 1b patient corrects severe neutropenia and recurrent infections.
4. There is a significant hematological effect and subjective improvement of infections after treatment with G-CSF.
5. Prolonged G-CSF is associated with complications and side effects among which bone pain and acute myeloid leukemia. Furthermore, GSD1b patients on G-CSF treatment should be carefully monitored for the risk of osteopenia/osteoporosis. The lowest effective G-CSF dose should be used to avoid spleno- megaly, hypersplenism, hepatomegaly, and bone pain.

6. The use of vitamin E and its effectiveness in reducing the frequency of infection and improving neutropenia in GSD Ib has been reported.

Summary Question answered:

Partly, several larger cohorts show treatment possibilities for neutropenia and infections. But there is limited evidence on the complications of treatment and when certain treatment is indicated. Should we include GSD Ia in this, since it has been asked or should we exclude this group?

Final Summary Question:

Merged:

What is the best therapy for neutropenia and infections (G-CSF or alternatives) considering outcomes, complications and side effects such as bone pain in patients with Glycogen Storage Disease Type Ib (or Ia)?

Merge between: G2IBD2 & G2IBD3
What is the optimal therapy (Modulen or alternatives) for Inflammatory Bowel Disease (IBD) and acute flares in patients with Glycogen Storage Disease Type Ib?

G2IBD2:
Is Modulen a viable treatment for Inflammatory Bowel Disease in patients with Glycogen Storage Disease Type Ib?

G2IBD3:
What is the therapeutic treatment in acute (flare) crohns in Glycogen Storage Disease Type Ib?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND “treatment”[tiab] AND “Inflammatory bowel disease”[tiab])

Found articles:
1. Neutropenia in glycogen storage disease Ib: outcomes for patients treated with granulocyte colony-stimulating factor. Dale DC, Bolyard AA, Marrero T, Kelley ML, Makaryan V, Tran E, Leung J, Boxer LA, Kishnani PS, Austin S, Wanner C, Ferrecchia IA, Khalaf D, Maze D, Kurtzberg J, Zeidler C, Welte K, Weinstein DA. PMID: 30451720 DOI: 10.1097/MOH.0000000000000474

1. Adalimumab for the treatment of Crohn-like colitis and enteritis in glycogen storage disease type Ib. Davis MK1, Rufo PA, Polyak SF, Weinstein DA. PMID: 18172743 DOI: 10.1007/s10545-007-0774-9.

2. Bone marrow transplantation in glycogen storage disease type 1b. Pierre G1, Chakupurakal G, McKiernan P, Hendriksz C, Lawson S, Chakrapani A. PMID: 18206704 DOI: 10.1016/j.jpeds.2007.09.031

3. Glycogen storage disease Ib and Crohn colitis in a young woman. Doko M1, Zjacic-Rotkvic V, Zovak M, Kopljar M, Glavan E, Radacic-Aumiler M. PMID: 11887936

Conclusion of articles:
1. G-CSF is effective to raise blood neutrophil counts and reduce fevers and infections in most patients. In conjunction with other therapies (salicylates, mesalamine sulfasalazine and prednisone), G-CSF ameliorates inflammatory bowel symptoms, but doses must be limited because it increases spleen size associated with abdominal pain

2. There is a significant hematological effect and subjective improvement of IBD after treatment with G-CSF.

3. In therapy resistant GSD Ib, if there is no response to G-CSF or 5-aminosaliclic acid, adalimumab can be tried for treatment of IBD as a case report demonstrated clinical and histological improvement.

4. A case report observed reduction in inflammatory bowel disease-related symptoms and improved metabolic control after bone marrow transplantation.
5. A case study has shown that in some cases hemicolectomy is performed after severe complications from inflammatory bowel disease

Summary Question answered:
No, there is limited evidence for treatment strategies for IBD in GSD Ib. Several treatment modalities are mentioned, but are not investigated in larger cohorts.

Final Summary Question:

Merged:

What is the optimal therapy (Modulen or alternatives) for Inflammatory Bowel Disease (IBD) and acute flares in patients with Glycogen Storage Disease Type Ib?

Code: G2Ade1

How do you prevent, monitor and manage adenomas in liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("Adenoma"[Mesh] OR “adenoma”[tiab]) AND (“prevent”[tiab] OR “monitor”[tiab] OR “manage”[tiab])

Found articles:

1. Title: Recent development and gene therapy for glycogen storage disease type Ia.
Authors: Chou JY, et al.
Year of publication: 2017
PMID: 29576889

2. Genereviews I, III and VI

3. Chou JY, Matern D, Mansfield BC, Chen YT. Type I glycogen storage diseases: disorders of the glucose-6-phosphatase complex. Curr Mol Med. 2002;2:121–143. [PubMed]

4. Chou JY, Jun HS, Mansfield BC. Glycogen storage disease type I and G6Pase-β deficiency: etiology and therapy. Nat Rev Endocrinol. 2010;6:676–688. [PMC free article] [PubMed]

5. Chou JY, Jun HS, Mansfield BC. Type I glycogen storage diseases: Disorders of the glucose-6-phosphatase/glucose-6-phosphate transporter complexes. J Inherit Metab Dis. 2015;38:511–519.

6. Labrune P, Trioche P, Duvaltier I, Chevalier P, Odièvre M. Hepatocellular adenomas in glycogen storage disease type I and III: a series of 43 patients and review of the literature. J Pediatr Gastroenterol Nutr. 1997;24:276–279. [PubMed]

7. Rake JP, Visser G, Labrune P, Leonard JV, Ullrich K, Smit GP. Glycogen storage disease type I: diagnosis, management, clinical course and outcome. Results of the European Study on Glycogen Storage Disease Type I (ESGSD I) Eur J Pediatr. 2002;161:S20–S34. [PubMed]

Conclusion of articles:

1. Dietary therapies for GSD-Ia are available, but cannot prevent the long-term complication of hepatocellular adenoma that may undergo malignant transformation to hepatocellular carcinoma. Animal models of GSD-Ia are now available and are being exploited to both delineate the disease more precisely and develop new treatment approaches, including gene therapy.
2. GSD I: In younger children (age <16 years), liver ultrasound performed at diagnosis and thereafter every 12 to 24 months. In affected individuals who are 16 years and older, liver computed tomography (CT) or magnetic resonance imaging (MRI) scanning using intravenous contrast should be done every six to 12 months to monitor for hepatic adenoma formation [Franco et al 2005]. Hepatic profile: serum AST, ALT, albumin, bilirubin, PT/INR, and aPTT, and creatinine every six to 12 months to monitor for liver damage When hepatic adenoma is

detected. Abdominal CT/MRI with contrast should be performed in older individuals or individuals within the pediatric age group once adenomas are detected on ultrasound. Imaging should be repeated every 6-12 months or more often depending on laboratory and clinical findings. Liver imaging studies (MRI/CT scan) should evaluate liver size, adenomas, evidence of portal hypertension, or features suggestive of liver carcinoma (nodules, heterogeneous echogenic shadows) [Franco et al 2005].

3. GSD III and VI: annually Liver ultrasound examination to screen for adenomas and evidence of liver scarring. MRI scans are limited to those individuals with abnormalities on the primary ultrasound screen.

Summary Question answered:
Partly. Prevention of hepatocellular adenoma is not always achieved with only dietary treatment. For GSD I, III and VI is a monitoring schedule of adenomas and how to screen.
I propose that we add “liver” adenomas to the question.

Final Summary Question:

The same:

How do you prevent, monitor and manage liver adenomas in liver Glycogen Storage Disease?

Code: G2Ade2
What are the predictors and diagnostics of malignant transformations of liver adenomas in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("malignant transformation"[tiab] OR “malignan*”[tiab] OR “transform*”[tiab])

Found articles:
1. Malignant transformation of hepatocellular adenoma with bone marrow metaplasia arising in glycogen storage disease type I: A case report. Iguchi T, Yamagata M, Sonoda T, Yanagita K, Fukahori T, Tsujita E, Aishima S, Oda Y, Maehara Y. PMID: 27900094. DOI: 10.3892/mco.2016.1034
2. Malignant Transformation of Hepatic Adenoma in Glycogen Storage Disease Type-1a: Report of an Exceptional Case Diagnosed on Surveillance Imaging. Baheti AD, Yeh MM, O'Malley R, Lalwani N. PMID: 26430540. DOI: 10.4103/2156-7514.163991
3. Identification of differentially expressed microRNAs in human hepatocellular adenoma associated with type I glycogen storage disease: a potential utility as biomarkers. Chiu LY, Kishnani PS, Chuang TP, Tang CY, Liu CY, Bali D, Koeberl D, Austin S, Boyette K, Weinstein DA, Murphy E, Yao A, Chen YT, Li LH. PMID: 24129885 DOI: 10.1007/s00535-013-0890-2

Conclusion of articles:
1. There are many case studies that demonstrate the development from HCA to HCC in GSD I, III and VI.
2. Malignant transformation of hepatocellular adenoma (HA) is relatively rare and has been reported to be associated with dysregulation of the β-catenin pathway. It is suggested that des-gamma-carboxy prothrombin may be an indicator of malignant transformation of hepatocellular adenoma.
3. Furthermore, other subtypes of hepacellular adenoma than the β-catenin-activated have been associated with hepatocellular carcinoma.
4. Several microRNAs, specifically miR-130b could serve as a circulating biomarker for detection of GSD Ia hepatocellular adenoma. There is speculation on different microRNAs that could be monitored for development and progression of liver tumors.

Summary Question answered:
No. Mostly case studies examine the transformation from HCA to HCC. Several factors that are associated with HCA or HCC are discussed, but not in a longitudinal sense.

Final Summary Question:

The same:

What are the predictors and diagnostics of malignant transformations of liver adenomas in patients with liver Glycogen Storage Disease?

Code: G2LT1
When should liver transplantation be considered in patients with liver Glycogen Storage Disease and what are the (dis)advantages?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("liver transplantation"[tiab])

Found articles:
1. Liver transplantation in glycogen storage disease type I. Boers SJ, Visser G, Smit PG, Fuchs SA. PMID: 24716823. DOI: 10.1186/1750-1172-9-47
2. Liver transplantation in patients with type IIIa glycogen storage disease, cirrhosis and hepatocellular carcinoma. Iglesias Jorquera E, Tomás Pujante P, Ruiz García G, Vargas Acosta ÁM, Pons Miñano JA. PMID: 30318896 DOI: 10.17235/reed.2018.5856/2018.
3. Liver transplantation for adenomatosis: European experience. PMID: 26919265 DOI: 10.1002/lt.24417

Conclusion of articles:
1. Liver transplantation has been discussed for some of the liver GSD subtypes (Ia, Ib, III, IV, VI and IX) and result in improved metabolic control and normal fasting tolerance after liver transplantation. Most complications seem to be the result of the liver transplantation procedure and subsequent immune suppression.
2. A large study on liver transplantation for adenomatosis in Europe (including GSD Ia) states that liver transplantation should remain an extremely rare treatment for adenomatosis, and should primarily concern the malignant transformation of adenomas.
3. Liver transplantation in GSD IV is still the primary mode of treatment.

Summary Question answered:
Partly. There is no consensus for the indications for liver transplantation for several types of GSD in literature. Furthermore, this has mostly been addressed in cross-sectional examinations.

Since G2LT2 is very similar to G2LT1, these questions can be added together by adding “and long-term outcomes” to the question.

Final Summary Question:

Merged:

When should liver transplantation be considered in patients with liver Glycogen Storage Disease and what are the (dis)advantages and long-term outcomes?

Code: G2LT2
How does liver transplantation modify the natural history of liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:

Found articles:
See G2LT1

Conclusion of articles:
-

Summary Question answered:
Since G2LT2 is very similar to G2LT1, these questions can be added together by adding "and long-term outcomes" to G2LT1.

Final Summary Question:

Merged.

See G2LT1

Code: G2Depr1
Is there a significant correlation between depression and liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:

Found articles:
See G1Com1l

Conclusion of articles:
See G1Com1l

Summary Question answered:
Partly. Since G1Com1l is about psychiatric problems and this includes depression, I propose to add these two questions together with the addition of “i.e. depression” to G1Com1l to not lose this specific information.

Final Summary Question:

Merged

See G1Com1l

Code: G2CD1
How does liver Glycogen Storage Disease affect the cognitive development of patients?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“cognition”[tiab] OR “cognitive”[tiab] OR “cognitive development”[tiab])

Found articles:
1. Cognitive profile of patients with glycogen storage disease type III: a clinical description of seven cases. Michon CC Gargiulo M, Hahn-Barma V, Petit F, Nadaj-Pakleza A, Herson A, Eymard B, Labrune P, Laforet P. PMID: 25388549 DOI: 10.1007/s10545-014-9789-1

Conclusion of articles:
1. Impairment of social cognition and executive functions is observed in GSD III patients. The studies hypothesizes about a central nervous system involvement in patients with GSD III.

Summary Question answered:
No. There is only one study that specifically focusses on GSD III and cognition at one time point. Should this question be merged with G2DD1 “Can liver Glycogen Storage Disease cause developmental delays throughout childhood?” or should these be seen as two separate questions?

Final Summary Question:

The same

How does liver Glycogen Storage Disease affect the cognitive development of patients?

Code: G2Com1
Which strategies could be useful to motivate adult patients with liver Glycogen Storage Disease to adhere to treatment?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“motivation”[tiab])

Found articles:
1. The adolescent with an inborn error of metabolism: medical issues and transition to adulthood. Enns GM, Packman W. PMID: 11986039

Conclusion of articles:
1. There are many difficulties when a patient has the transition to adulthood, among which motivation to adhere to treatment. In the abovementioned opinionated article it is discussed that education and knowledge on disease and treatment is essential.

Summary Question answered:
No. Only one opinionated article discusses this problem.

Final Summary Question:

The same:

Which strategies could be useful to motivate adult patients with liver Glycogen Storage Disease to adhere to treatment?

Code: G2Psy1
How does liver Glycogen Storage Disease affect patients and families psychologically?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“psychosocial*”[tiab])

Found articles:
1. Psychosocial functioning in youth with glycogen storage disease type I. Storch E, Keeley M, Merlo L, Jacob M, Correia C, Weinstein D. PMID: 18296725 DOI: 10.1093/jpepsy/jsn017

2. The adolescent with an inborn error of metabolism: medical issues and transition to adulthood. Enns GM, Packman W. PMID: 11986039

Conclusion of articles:
1. Children with GSD Type Ia and Ib were rated as having more internalizing symptoms, social problems, and lower independent functioning relative to healthy controls. Parents reported greater distress and parenting stress relative to healthy controls.

2. There are many difficulties when a patient has the transition to adulthood, among which motivation to adhere to treatment. In the abovementioned opinionated article it is discussed that education and knowledge on disease and treatment is essential.

Summary Question answered:
No. The psychosocial functioning has only been studied for GSD I and in one opiniated article.

Final Summary Question:

How does liver Glycogen Storage Disease affect patients and families psychologically?

Summary Questions Group 3

Code: G3Sup1

What is the need for supplementation of micronutrients (such as vitamins and calcium) in patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("dietary supplements"[Mesh] OR "supplementation"[tiab] OR "dietary supplement*"[tiab]) AND ("micronutrients"[Mesh] OR "micronutrients"[tiab] OR "vitamin"[tiab] OR "calcium"[tiab])

Found articles:

1. Title: Decreased urinary citrate excretion in type 1a glycogen storage disease.
   Authors: Weinstein DA, et al.
   Year of publication: 2001
   PMID: 11241046
2. Title: Vitamin E supplementation improves neutropenia and reduces the frequency of infections in patients with glycogen storage disease type 1b.
   Authors: Melis D, et al.
   Year of publication: 2009
   PMID: 19066956
3. Title: Hypovitaminosis D in glycogen storage disease type I.
   Authors: Banugaria SG, et al.
   Year of publication : 2010
   PMID : 20060350
4. Title: Nutritional therapy for GSD
   Authors: Heller S, et al.
   Year of publication: 2008
   DOI: 10.1097/MPG.0b013e3181818ea
5. ACMG
6. ESGSDI
7. IGSDIII
8. Genereviews GSDI

Conclusion of articles:

1. Citrate supplementation may be beneficial in preventing or ameliorating nephrocalcinosis and the development of urinary calculi in GSD1a.
2. GSD Ib: During vitamin E supplementation, the mean values of neutrophil counts were significantly higher ($p < 0.05$) and neutrophil counts lower than 500/mm3 were found less frequently ($p < 0.05$); the frequency and severity of infections, mouth ulcers and perianal lesions, was reduced ($p < 0.05$); ileocolonoscopy and histology showed a mild improvement. Vitamin E supplementation did not result in changes in neutrophil function. In conclusion, our study suggests a role of vitamin E supplementation at least as an adjunct therapy of GSD1b to reduce G-CSF doses or the frequency of G-CSF administration. Vitamin E has evident advantages as compared to G-CSF, as it can be assumed orally, and it has not been associated with severe side effects.
3. Vitamin D deficiency in GSD I. Based on recommendations by Holick et al., adult patients with low 25(OH)D levels should be treated with 50,000 IU (4,000 IU daily for

children) of vitamin D_2 once weekly for 8 weeks with subsequent reevaluation of 25(OH)D levels. At this time, if the level is in the normal range, the patient may begin a maintenance dose of 1000 IU vitamin D daily or, alternatively, 50,000 IU vitamin D every other week [16]. One of the patients (Patient 1) with severe vitamin D deficiency (25(OH)D level – 8.8 ng/ml) was started on the above-mentioned therapeutic dose of vitamin D_2 for eight weeks, after which her total 25(OH)D level was 30.1 ng/ml with significant improvement in 25(OH)D_2 level from less than 4.0 ng/ml to 22.6 ng/ml.

4. Supplementation with a multivitamin-mineral supplement, including calcium, is required because of the limited intake of milk and fruits.
5. Restricting fruit, juice, and dairy foods impacts two entire food groups and renders the diet inadequate. In GSD I, a complete multivitamin with minerals is essential. If a sugar-free soy- based milk that is fortified with calcium and vitamin D is not included, then calcium with vitamin D supplements are also essential. Without appropriate supplements, these children are at risk for a variety of nutritional deficiencies
6. Special attention is needed regarding calcium (limited milk intake) and vitamin D. Further- more, increased carbohydrate metabolism needs sufficient vitamin B1.
7. because all food groups are allowed on the diet for GSD IIIa and IIIb, vitamin and mineral supplements are only prescribed based on individual need.
8. GSD I: Calcium and vitamin D supplements to support bone growth and mineralization. If the individual is not on calcium-fortified soy milk, calcium citrate or calcium carbonate with vitamin D is recommended to meet RDA for age needs and to prevent nutritional deficiency

Summary Question answered:

Partly. In GSD I calcium, citrate and Vitamin D supplements are needed. And increased carbohydrate metabolism needs sufficient vitamin B1. For GSD III it is based on the individual needs. For other GSD types there is limited research. Furthermore, this is difficult to answer based on the nature of the question and the cultural, social and economical differences. This should be investigated in an international cohort to provide an answer for the entire liver GSD community.

Final Summary Question:

The same:

What is the need for supplementation of micronutrients (i.e. vitamins and calcium) in patients with liver Glycogen Storage Disease?

Code: G3MCT1

Which is the role and use of MCT in the management of different patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“medium chain triglyceride diet”[tiab])

Found articles:

1. Title: Glycogen storage disease type 1: impact of medium-chain triglycerides on metabolic control and growth.
Authors: Das AM, et al.
Year of publication: 2010
PMID: 20357432
2.Title: Improvements of hypertriglyceridemia and hyperlacticemia in Japanese children with glycogen storage disease type Ia by medium-chain triglyceride milk.
Authors: Nagasaka H, et al.
Year of publication: 2007
PMID: 17206455

Conclusion of articles:

1. The MCT diet led to a decrease in uric acid concentrations in all patients. Triglyceride levels were reduced only in the youngest patient, while lactate concentrations did not significantly decrease. The MCT diet allowed for a reduction in carbohydrate and caloric intake required to maintain euglycaemia and led to improvement in growth in the two prepubertal patients.
2. The present study showed that MCT milk exerts the effects to lower blood triglyceride levels and to raise HDL cholesterol levels in our patients. All patients were homozygous for G747T mutation, which is highly preva- lent among Japanese patients and is associated with a somewhat milder phenotype. Therefore, whether the results obtained from our patients could be applied to other patients with different mutations must be explored.

Summary Question answered:

Partly**.** There is however much debate in literature on the effect and indication of MCT supplementation in different liver GSD types and differences between patients. This is based on case studies and smaller group studies and there is a need for more data and randomized trials to further investigate this subject. I suggest to write the abbreviation MCT in full.

Final Summary Question:

The same:

Which is the role and use of medium-chain triglycerides (MCT) in the management of different patients with liver Glycogen Storage Disease?

Code: G3KD1

What are the effects of different kinds of Ketogenic Diet in patients with Glycogen Storage Disease Type III?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("Diet, Ketogenic"[Mesh] OR “ketogenic diet”[tiab])

Found articles:

1. Title: Successful Treatment of Severe Cardiomyopathy in Glycogen Storage Disease Type III With D,L-3-Hydroxybutyrate, Ketogenic and High-Protein Diet
Authors: Vassili Valayannopoulos, et al.
Year of publication : 2011
DOI: 0031-3998/11/7006-0638
1. Title: Improvement of cardiomyopathy after high-fat diet in two siblings with GSD type III
Authors: Brambilla A, et al.
Year of publication: 2014
PMID: 25308556
2. Title: Lipids in hepatic glycogen storage diseases: pathophysiology, monitoring of dietary management and future directions
Authors: Derks TGJ, et al.
Year of publication:2015
PMID: 25633903

Conclusion of articles:

1. In conclusion, we report on a new treatment concept of GSD III with D,L-3-hydroxybutyrate, ketogenic and high protein diet which was associated with an improvement of cardiomyopathy, a severe and fatal complication of the disease that occurred in our patient’s sibling. However, as this is a single patient study, we cannot affirm that our findings are solely due to our therapeutic interventions and could not be related to the variability of the disease even within the same family. These encouraging data need thus to be confirmed in more GSD III patients with cardiomyopathy or muscular symptoms.
2. A diet rich in fats as well as proteins and poor in carbohydrates could be a beneficial therapeutic choice for GSD III with cardiomyopathy. Future research is needed to confirm the beneficial effect of this treatment and to design treatment strategies with the aim to provide alternative source of energy and prevent glycogen accumulation.
3.There are no experimental data to substantiate whether long-term dietary MCT may cause liver adenoma and hepatocellular carcinoma

Summary Question answered:

No. The found studies are only case studies and expert opinion.

Final Summary Question:

The same:

What are the effects of different kinds of Ketogenic Diet in patients with Glycogen Storage Disease Type III?

Code: G3DR1

What is the needed restriction of lactose, fructose or saccharose in different types of liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("lactose"[Mesh] OR "lactose"[tiab] OR "fructose"[Mesh] OR "fructose"[tiab] OR "sucrose"[Mesh] OR "sucrose"[tiab] OR "saccharose"[tiab] OR "monosaccharides"[Mesh] OR "monosaccharides"[tiab]) AND ("restriction"[tiab])

Found articles:

1. Title: Nutritional therapy for GSD
   Authors: Heller S, et al.
   Year of publication: 2008
   DOI: 10.1097/MPG.0b013e3181818ea
2. ACMG
3. IGSDIII
4. Genereviews GSD I and III

Conclusion of articles:

1. basis of nutritional therapy is feeding GSD type I patients with foods rich in starches with low concentrations of galactose and fructose during the day and to prevent hypoglycemia during the night. Foods that contain galactose and fructose, such as fruits, milk, and sugar, should be limited or avoided because of their conversion to glycogen and lactate and also because they may contribute to the development of lactic acidosis.

2. GSD I: As a result of the deficiency of the G6Pase enzyme, fructose and galactose are not metabolized to glucose-6-phosphate, which further contributes to the biochemical abnormalities. There is no consensus regarding the restriction of these two sugars in the diet, but sucrose (fructose and glucose) and lactose (galac- tose and glucose) are often limited or avoided. Limiting these sugars reduces or completely eliminates sugar, fruit, juice, dairy, and foods that contain these products from the diet

3. GSD III: Because gluconeogenesis is intact in GSD III, sucrose, fruc- tose, and lactose are not restricted as they are for individuals with GSD I. However, simple sugars are discouraged in favor of a diet that is higher in complex carbohydrates and protein and to reduce glycogen storage.

4.Intake of sucrose and fructose should be restricted for infants and older children. Avoid sugar, fruits, fruit juice, high-fructose corn syrup, sorbitol, cane juice, and other foods that cannot be broken down into glucose. (2) Intake of lactose and galactose should be limited. One serving per day for an older child usually entails 1.5 ounces of cheese OR 1 cup of yogurt OR 1 cup of skim milk.

Summary Question answered:

Partly. There is however no international consensus for the answer to this question. More mechanistical and clinical studies should be performed to gain insights into this question and to write guidelines to answer the question.

Final Summary Question:

The same:

What is the needed restriction of lactose, fructose or saccharose in different types of liver Glycogen Storage Disease?

Code: G3PE1
How to manage diet regimen in relation to “before, during and after” physical exercise (sport, playing) for patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("Diet"[Mesh] OR “exercise”[tiab]) AND (“exercise”[Mesh] OR “exercise”[tiab] OR “physical”[tiab])

Found articles:
1. ACMG

2. IGSDIII

3. Genereviews GSD IX

Conclusion of articles:
1. Patients should be encouraged to participate in age-appropriate physical activities, but contact or competitive sports should be avoided because of the risk of liver injury.

2. As a general rule, no exercise restrictions are recommended for individuals with GSD III. Although exercise restrictions may be necessary if significant ventricular hypertrophy with ventricular outflow tract obstruction develops or if heart rhythm abnormalities develop (also see section on Physical therapy/ exercise).

3. GSD type IX Little published information is available on prevention of primary manifestations in individuals with muscle PhK deficiency; however, regular moderate aerobic exercise may be beneficial. Intense exercise should be avoided as it may promote rhabdomyolysis and muscle cramping. Regular evaluation by a physical therapist to look for progression in symptoms and to guide exercise program

Summary Question answered:
No. There is insufficient data in clinical trials to properly address this question.

Final Summary Question:

The same:

How to manage diet regimen in relation to “before, during and after” physical exercise (sport, playing) for patients with liver Glycogen Storage Disease?

Code: G3DT1
What are the long term complications (liver, renal, gut) of a diet rich in UCCS (or Glycosade) and/or high protein and should the diet be adjusted to prevent complications in the different liver Glycogen Storage Diseases?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“high protein”[tiab] OR “glycosade”[tiab] OR “uncooked cornstarch”[tiab] OR “uncooked corn starch”[tiab] OR “overtreatment”[tiab]) AND ("complications"[tiab] OR "outcome"[tiab])

Found articles:
1. Title: A lower energetic, protein and uncooked cornstarch intake is associated with a more severe outcome in glycogen storage disease type III: an observational study of 50 patients
Authors: Chehida AB, et al.
Year of publication : 2018
PMID: 30110253

2. Title: Glycogen storage disease type III: diagnosis, genotype, management, clinical course and outcome
Authors: Sentner CP, et al.
Year of publication: 2016
PMID: 27106217

3. Lipids in hepatic glycogen storage diseases: pathophysiology, monitoring of dietary management and future directions
Authors: Derks TGJ, et al.
Year of publication: 2015
PMID: 25633903

4. The natural history of glycogen storage disease types VI and IX: Long-term outcome from the largest metabolic center in Canada
Authors: Roscher A, et al.
Year of publication: 2014
PMID: 25266922

5.The effect of tailoring of cornstarch intake on stature in children with glycogen storage disease type III
Authors: El-Karaksy H, et al.
Year of publication: 2015
PMID:25153581

6. Aggressive Therapy Improves Cirrhosis in Glycogen Storage Disease Type IX
Authors: Tsilianidis LA, et al.
Year of publication : 2013
PMID: 23578772

7. Reversal of glycogen storage disease type IIIa-related cardiomyopathy with modification of diet
Authors: Dagli AI, et al.
Year of publication 2009
PMID: 19322675

Conclusion of articles:

1. A low caloric, protein and uncooked cornstarch intake is associated with a more severe outcome in GSDIII Tunisian patients. Neuromuscular and CIs were particularly precocious and severe, even in childhood.
2. GSD III: hypothesized that carbohydrate overtreatment may be an important risk factor for cardiac involvement and/or cardiomyopathy.
3. Future experimental animal studies and well-designed collaborative dietary intervention studies are necessary to improve our understanding about manipulations in macronutrients, like the restrictions of simple sugars, traditional versus heat-treated modified starch, the role of protein, MCT-treatment, triheptanooin and the ketogenic diet in GSD type III.
4. High protein diet is recommended to arrest progression of the disease or improve muscle function in GSD-VI. Further controlled studies of the possible benefit of therapeutic interventions including uncooked cornstarch and high protein diet are necessary
5. Adjusting the intervals between the cornstarch doses for each patient with GSD III, according to individual fasting tolerance test was very beneficial and resulted in improvement of the linear growth velocity and reduction in the frequency of hypoglycemic seizures as well as the size of the liver. Individual scheduling of cornstarch doses prevents complications in those who develop hypoglycemia at short intervals; it also allows some relaxation in schedule for those who can tolerate longer fasting hours to improve their appetite and prolong their uninterrupted sleep hours.
6. GSDIXa: Even in patients with a less severe presentation, consideration of a structured treatment regimen to improve quality of life appears warranted. Structured therapy with frequent doses of uncooked cornstarch and protein supplementation was initiated, and both children responded with improved growth velocity, increased energy, decreased hepatomegaly and improved well-being.
7. IIIA: This case report demonstrates that a diet providing 30% of energy from protein and avoidance of over-treatment with carbohydrate can stabilize and even reverse cardiomyopathy.

8. III: CS was decreased to just enough to maintain normal glycemia. A dramatic improvement in his cardiomyopathy was observed, suggesting that a high protein diet without overtreating with CS can reverse and possibly prevent cardiomyopathy
9. I: Other complications of overfeeding, including increased glycogen storage, over time can lead to hyperinsulinemia and insulin resistance. Excess CS or taking CS too close to meal time reduces the appetite at meal time, limiting the intake of nutritious foods, and can result in nutrient deficiencies. Overtreatment can also lead to worsening lactic acidosis. Increased gastrointestinal disturbances may also result from excess CS. Scheduling CS and balancing meals can be difficult and the metabolic dietitian should work closely with the family early on to avoid the development of feeding issues.

Summary Question answered:
Partly.

GSD I: increased glycogen storage, hyperinsulinemia, insulin resistance, reduces the appetite at meal time can result in nutrient deficiencies, worsening lactic acidosis and increased gastrointestinal disturbances.

GSD III: risk factor for cardiac involvement and/or cardiomyopathy.

Since the liver GSD population is ageing, many complications may still be obscured. Furthermore, there is much data not present on the other liver GSD types. I added a few textual changes to the question.

Final Summary Question:

The same:

What are the long-term complications (liver, renal, gut) of a diet rich in uncooked cornstarch and/or high protein and should the diet be adjusted to prevent complications in liver Glycogen Storage Diseases?

Code: G3DT2
Can guidelines be made for patients with liver Glycogen Storage Disease and their caregivers about how to deal with behavioral problems and management of GSD diet, such as social consequences, lack of appetite/eating refusal, motivation, and sleeping disorders?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“Problem Behavior"[Mesh] OR “social consequences”[tiab] OR “lack of appetite”[tiab] OR “eating problems”[tiab] OR “sleeping disorders"[tiab] OR "sleeping problems"[tiab] OR “sleeping”[tiab] OR “quality of life”[tiab])

Found articles:
1. Sleep and quality of life of patients with glycogen storage disease on standard and modified uncooked cornstarch
Authors: Rousseau-Nepton I, et al.
Year of publication : 2018
PMID: 29223626

Conclusion of articles:
1. Prior to the intervention, we showed poor quality of sleep with frequent awakenings, but a normal duration of sleep in adults with GSD Ia. The sleep quality in the post intervention group had improved to the normal range and this was a statistically significant difference.

2. Excess CS or taking CS too close to meal time reduces the appetite at meal time, limiting the intake of nutritious foods, and can result in nutrient deficiencies

Summary Question answered:
No. There are no guidelines available on how parents can deal with liver GSD diet and the abovementioned problems.

Final Summary Question:

The same:

Can guidelines be made for patients with liver Glycogen Storage Disease and their caregivers about how to deal with behavioral problems and management of GSD diet, such as social consequences, lack of appetite/eating refusal, motivation, and sleeping disorders?

Code: G3DT3

Which is the best way to administer the diet and should a gastrostomy be placed for patients with liver Glycogen Storage Disease? Bolus corn-Starch vs. nasogastric tube feeding in terms of long term complication, quality of life, type of GSD, glucose responsiveness and finding optimal dose of carbohydrates.

Search Strategy

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("uncooked cornstarch"[tiab] OR "dripfeeding"[tiab])
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Found articles:

1. Feeding Difficulties and Orofacial Myofunctional Disorder in Patients with Hepatic Glycogen Storage Diseases.
Martinez CC, Tonon T, Nalin T, Refosco LF, de Souza CFM, Schwartz IVD.
JIMD Rep. 2018 Sep 22. doi: 10.1007/8904_2018_131. [Epub ahead of print]
PMID: 30242630
2. The effect of tailoring of cornstarch intake on stature in children with glycogen storage disease type III.
El-Karaksy H, El-Raziky MS, Anwar G, Mogahed E.
J Pediatr Endocrinol Metab. 2015 Jan;28(1-2):195-200. doi: 10.1515/jpem-2014-0145.
PMID: 25153581
3. Dietary treatment of glycogen storage disease type Ia: uncooked cornstarch and/or continuous nocturnal gastric drip-feeding?
Derks TG, Martens DH, Sentner CP, van Rijn M, de Boer F, Smit GP, van Spronsen FJ.
Mol Genet Metab. 2013 May;109(1):1-2. doi: 10.1016/j.ymgme.2013.02.005. Epub 2013 Feb 15. No abstract available.
PMID: 23480859

Conclusion of articles:

1. There is much debate on the preference for and effects of dripfeeding and cornstarch dosis in literature.
2. For patients with GSD Ib and neutropenia, a G-tube may not be a good option because of the risk for recurrent infections at the surgical site. If a child has neutropenia, a G-tube should be placed only if granulocyte colony-stimulating factor (G-CSF) (Neupogen) is being administered.
3. Access via NG or G-tube placement is recommended for emergencies and/or for OGFs

Summary Question answered:

Partly. There is a lack of a systematic analysis of larger groups of patients. I propose we change the question to make it more understandable. The mentioned options in the questions are very useful for a future development of a research question, but for simplicity I believe we can better adapt the question. We are already discussing the complications of dietary management in general in question G3DT1. Glucose responsiveness is a complication of treatment. We are already discussing age-related therapy in question G3DT5. I would focus the question on the start of dietary management, finding the optimal doses and how to administer the diet.

Final Summary Question:

Changed:

What is the best way to start dietary treatment, finding the optimal doses, and to administer the diet for patients with liver Glycogen Storage Disease?

Code: G3DT4

Is there any research of modification of the existing cornstarch preparations, and in alternative treatments that can keep blood glucose stable for longer time and be easier to administer for patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“alternative treatment”[tiab] OR "alternative"[tiab]) AND (“cornstarch”[tiab])

Found articles:

1. Title: Use of modified cornstarch therapy to extend fasting in glycogen storage disease types Ia and Ib Authors: Correia C, et al. Year of publication: 2013. PMID: **18996862**

Conclusion of articles:

1. Our study showed improved prevention of hypoglycemia, a slowed rate of increase in blood sugar, and a slowed rate of blood glucose fall with the experimental cornstarch (Glycosade) compared with the currently used product. But no significant difference was found in lactate concentrations between the cornstarch preparations. Future studies are warranted to determine whether alternative dosing will improve control in the therapeutic range.

Summary Question answered:

Partly. I propose we adapt the question to keep it more simple.

Final Summary Question:

Changed:

How can existing cornstarch preparations be modified or alternative treatments be implemented that are easier to administer and/or keep blood sugar levels more stable for patients with liver Glycogen Storage Disease?

Code: G3DT5

What is the optimal diet in concern of macro-/micronutrients and amount of carbohydrates and proteins for the different types of GSD, at different age and in different situations? And how often should the diet be adjusted?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“optimal diet"[Mesh] OR “optimal diet”[tiab] OR “diet”[tiab])

Found articles:

1. Genereviews GSD I and III

Conclusion of articles:

GSD I

Complex carbohydrates (60%-70% of recommended total energy intake) including cornstarch and starches from whole-grain bread, rice, and potatoes for children and adolescents and rice cereals for infants
Note: Intake of sucrose and fructose should be restricted for infants and older children. Avoid sugar, fruits, fruit juice, high-fructose corn syrup, sorbitol, cane juice, and other foods that cannot be broken down into glucose. Intake of lactose and galactose should be limited. One serving per day for an older child usually entails 1.5 ounces of cheese OR 1 cup of yogurt OR 1 cup of skim milk. Blood glucose monitoring for hypoglycemia is important so that overtreatment with cornstarch may be avoided. If excess weight gain occurs, consider decreasing the amount of cornstarch gradually over time and mixing cornstarch in water instead of Prosobee® or Tolerex®.
Protein (10%-15% of recommended total energy intake) of high quality, high biologic value (e.g., protein low in fat). Soy formula (Prosobee®) and soy milk (lactose/galactose free) can be used both in infancy and childhood for carbohydrate and protein needs.
Note:Avoid soy milks that are sweetened with sucrose; the ones with rice syrup or brown rice syrup can be taken. Soy milk mixed with cane sugar should be avoided.
Fat (10%-15% of recommended total energy intake) as part of a low-fat diet that includes heart-healthy fats such as canola oil and olive oil. Note: Families need explicit guidelines on fat intake as part of monitoring total energy intake and avoiding excessive weight gain.

GSD III: A high-protein diet and frequent feeds (every three to four hours) to maintain euglycemia is the mainstay of management in infancy. Fructose and galactose can be used; special formulas are not required. Toward the end of the first year of life, one to three daily doses of 1g/kg cornstarch can be used to avoid hypoglycemia. A protein intake of 3g/kg is recommend

Summary Question answered:

Partly. There are many studies into dietary management, but not for all types of liver GSD and not as randomized controlled clinical trials. I propose we simplify the question.

Final Summary Question:

Changed:

How can we individualize the diet and the adjustment regarding macronutrients (fats, carbohydrates, proteins) and micronutrients for patients with liver Glycogen Storage Disease?

Summary Questions Group 4

Code: G4MC1
How does dietary intake impact on metabolic control in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:
Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND "diet"[tiab] AND "metabolic control"[tiab])

Found articles:

1.Glucose-free/high-protein diet improves hepatomegaly and exercise intolerance in glycogen storage disease type III mice. Pagliarani S, et al. Biochim Biophys Acta Mol Basis Dis. 2018 Oct;1864(10):3407-3417. doi: 10.1016/j.bbadis.2018.07.031. Epub 2018 Aug 1. PMID: 30076962
2. Hepatic glycogen storage disorders: what have we learned in recent years? Burda P, Hochuli M. Curr Opin Clin Nutr Metab Care. 2015 Jul;18(4):415-21. doi: 10.1097/MCO.0000000000000181. Review. PMID: 26001652
3. Dietary dilemmas in the management of glycogen storage disease type I. Bhattacharya K. J Inherit Metab Dis. 2011 Jun;34(3):621-9. doi: 10.1007/s10545-011-9322-8. Epub 2011 Apr 14. Review. PMID: 21491105.
4. Glycogen storage disease type 1: impact of medium-chain triglycerides on metabolic control and growth. Das AM, Lücke T, Meyer U, Hartmann H, Illsinger S. Ann Nutr Metab. 2010;56(3):225-32. doi: 10.1159/000283242. Epub 2010 Mar 30. PMID: 20357432.

Conclusion of articles:

1. A glucose free/high protein diet improves hepatomegaly and exercise intolerance in GSD III mice and did not ameliorate biochemical control in comparison with high-protein diet with carbohydrates only.
2. More controlled prospective studies are needed to assess effects of different dietary and medical treatment options on biochemical outcomes.
3. Regular clinical and dietary review is imperative as patients grow, ensuring adequate but not excessive low glycaemic index carbohydrate intake, appropriate dynamic biochemical profiles and suitable age appropriate eating patterns
4. MCT supplementation had a positive effect on metabolic control and growth in our patients suffering from GSD 1.

Summary Question answered:
No, this questions has not been sufficiently addressed in prospective cohorts with different types of standardized diets.

Final Summary Question:

The same:

How does dietary intake impact on metabolic control in patients with liver Glycogen Storage

Disease?

Code: G4DT1
What testing should be performed on a daily basis in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND “test*"[tiab] OR “daily”[tiab])

Found articles:
None of additional relevance.

Conclusion of articles:
-

Summary Question answered:
I propose we merge this question with G4Mon1 below.

Final Summary Question:

Merged:

See G4Mon1.

Code: G4Mon1
What laboratory testing and with which frequency is beneficial for monitoring patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("Laboratory tests" [tiab] OR "Biochemical parameters"[tiab])

Found articles:

1. Clinical and biochemical heterogeneity between patients with glycogen storage disease type IA: the added value of CUSUM for metabolic control. Peeks F, Steunenberg TAH, de Boer F, Rubio-Gozalbo ME, Williams M, Burghard R, Rajas F, Oosterveer MH, Weinstein DA, Derks TGJ. J Inherit Metab Dis. 2017 Sep;40(5):695-702. doi: 10.1007/s10545-017-0039-1. Epub 2017 Apr 10. PMID: 28397058

Conclusion of articles:
1. Based on previous large cohorts of GSD I and III guidelines have been made for laboratory testing. These are not follow-up studies. In smaller series there are advices based on case reports for other GSD types.
2. Laboratory testing can differ for patients that have developed complications, such as liver adenomas.
3. Laboratory testing could be individualised since there is large heterogeneity between patients with liver GSD.

Summary Question answered:
Partly this question has been addressed, but not for prospective cohorts and larger studies for non GSD I or III are necessary. I propose we merge this question with G4DT1 with putting “laboratory” between brackets.

Final Summary Question:

Merged:

What (laboratory) testing and with which frequency is optimal for monitoring patients with liver Glycogen Storage Disease?

Code: G4Tar1
What are the target levels for metabolic testing in liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("target*" [tiab])

Found articles:
1. Clinical and biochemical heterogeneity between patients with glycogen storage disease type IA: the added value of CUSUM for metabolic control. Peeks F, Steunenberg TAH, de Boer F, Rubio-Gozalbo ME, Williams M, Burghard R, Rajas F, Oosterveer MH, Weinstein DA, Derks TGJ. J Inherit Metab Dis. 2017 Sep;40(5):695-702. doi: 10.1007/s10545-017-0039-1. Epub 2017 Apr 10. PMID: 28397058
2. Type I glycogen storage disease: favourable outcome on a strict management regimen avoiding increased lactate production during childhood and adolescence. Däublin G, Schwahn B, Wendel U. Eur J Pediatr. 2002 Oct;161 Suppl 1:S40-5. Epub 2002 Aug 22. PMID: 12373569
3. Effect of continuous glucose therapy with uncooked cornstarch on the long-term clinical course of type 1a glycogen storage disease. Weinstein DA, Wolfsdorf JI. Eur J Pediatr. 2002 Oct;161 Suppl 1:S35-9. Epub 2002 Jul 31. PMID: 12373568

Conclusion of articles:
1. Based on previous large cohorts of GSD I and III guidelines have been made for metabolic targets. The follow-up studies are few and contain only a small sample size. In smaller series there are advices based on case reports for other GSD types.
2. Not much is known about long-term complications of patients with liver GSD.
3. There is much debate on adequate target levels below or above which complications occur, such as hypoglycaemia.
4. Target levels of different metabolic components influence each other. For example, to avoid increased lactate production, glucose concentrations often remain in the high normal range.

Summary Question answered:
Partly this question has been addressed, but not for prospective cohorts. Larger studies for non GSD I or III are necessary.

Final Summary Question:

The same:

What are the target levels for metabolic testing in liver Glycogen Storage Disease?

Code: G4Lab1

How should optimal metabolic control both clinically and biochemically (like lactate, ketones and/or lipids) be achieved in liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("target*" [tiab])

Found articles:

1. Tight metabolic control plus ACE inhibitor therapy improves GSD I nephropathy. Okechuku GO, Shoemaker LR, Dambska M, Brown LM, Mathew J, Weinstein DA. J Inherit Metab Dis. 2017 Sep;40(5):703-708. doi: 10.1007/s10545-017-0054-2. Epub 2017 Jun 13. PMID: 28612263.
2. Prevention of complications in glycogen storage disease type Ia with optimization of metabolic control. Dambska M, Labrador EB, Kuo CL, Weinstein DA. Pediatr Diabetes. 2017 Aug;18(5):327-331. doi: 10.1111/pedi.12540. Epub 2017 Jun 1. Review. PMID: 28568353
3. Clinical and biochemical heterogeneity between patients with glycogen storage disease type IA: the added value of CUSUM for metabolic control. Peeks F, Steunenberg TAH, de Boer F, Rubio-Gozalbo ME, Williams M, Burghard R, Rajas F, Oosterveer MH, Weinstein DA, Derks TGJ. J Inherit Metab Dis. 2017 Sep;40(5):695-702. doi: 10.1007/s10545-017-0039-1. Epub 2017 Apr 10. PMID: 28397058
4. Hepatic glycogen storage disorders: what have we learned in recent years? Burda P, Hochuli M. Curr Opin Clin Nutr Metab Care. 2015 Jul;18(4):415-21. doi: 10.1097/MCO.0000000000000181. Review. PMID: 26001652
5. Disordered Eating and Body Esteem Among Individuals with Glycogen Storage Disease. Flanagan TB, Sutton JA, Brown LM, Weinstein DA, Merlo LJ. JIMD Rep. 2015;19:23-9. doi: 10.1007/8904_2014_359. Epub 2015 Feb 10. PMID: 25665833
6. Progression of renal damage in glycogen storage disease type I is associated to hyperlipidemia: a multicenter prospective Italian study. Melis D, Cozzolino M, Minopoli G, Balivo F, Parini R, Rigoldi M, Paci S, Dionisi-Vici C, Burlina A, Andria G, Parenti G. J Pediatr. 2015 Apr;166(4):1079-82. doi: 10.1016/j.jpeds.2014.12.015. Epub 2015 Jan 29. PMID: 25641239
7. Regression of hepatocellular adenomas with strict dietary therapy in patients with glycogen storage disease type I. Beegle RD, Brown LM, Weinstein DA. JIMD Rep. 2015;18:23-32. doi: 10.1007/8904_2014_344. Epub 2014 Oct 12. PMID: 25308557.
8. Impaired bone metabolism in glycogen storage disease type 1 is associated with poor metabolic control in type 1a and with granulocyte colony-stimulating factor therapy in type 1b. Melis D, Pivonello R, Cozzolino M, Della Casa R, Balivo F, Del Puente A, Dionisi-Vici C, Cotugno G, Zuppaldi C, Rigoldi M, Parini R, Colao A, Andria G, Parenti G. Horm Res Paediatr. 2014;81(1):55-62. doi: 10.1159/000351022. Epub 2013 Dec 21. PMID: 24401800.
9. Glycogen storage disease type Ia: linkage of glucose, glycogen, lactic acid, triglyceride, and uric acid metabolism. Sever S, Weinstein DA, Wolfsdorf JI, Gedik R, Schaefer EJ. J Clin Lipidol. 2012 Nov-Dec;6(6):596-600. doi: 10.1016/j.jacl.2012.08.005. Epub 2012 Aug 30. PMID: 23312056

10. Dietary dilemmas in the management of glycogen storage disease type I. Bhattacharya K. J Inherit Metab Dis. 2011 Jun;34(3):621-9. doi: 10.1007/s10545-011-9322-8. Epub 2011 Apr 14. Review. PMID: 21491105
11. Hyperlipidemia in glycogen storage disease type III: effect of age and metabolic control. Bernier AV, Sentner CP, Correia CE, Theriaque DW, Shuster JJ, Smit GP, Weinstein DA. J Inherit Metab Dis. 2008 Dec;31(6):729-32. doi: 10.1007/s10545-008-0919-5. Epub 2008 Aug 19. PMID: 18709545
12. Metabolic control and renal dysfunction in type I glycogen storage disease. Wolfsdorf JI, Laffel LM, Crigler JF Jr. J Inherit Metab Dis. 1997 Aug;20(4):559-68. PMID: 9266393.
13. Optimal rate of enteral glucose administration in children with glycogen storage disease type I. Schwenk WF, Haymond MW. N Engl J Med. 1986 Mar 13;314(11):682-5. PMID: 3081806
14. Aggressive therapy improves cirrhosis in glycogen storage disease type IX. Tsilianidis LA, Fiske LM, Siegel S, Lumpkin C, Hoyt K, Wasserstein M, Weinstein DA. Mol Genet Metab. 2013 Jun;109(2):179-82. doi: 10.1016/j.ymgme.2013.03.009. Epub 2013 Mar 21. PMID: 23578772

Conclusion of articles:
1. Optimal/Tight metabolic control seems to prevent complications from occurring.
2. For some patients it is more difficult to achieve optimal metabolic control then others, due to intrinsic or extrinsic factors.
3. There is much debate on the social consequences of dietary therapy necessary for optimal metabolic control.

Summary Question answered:
Partly, there is evidence that optimal metabolic control leads to prevention of complications. There are more studies necessary in how this can be achieved and what the consequences are of optimal metabolic control. I suggest a small textual change “such as” to “i.e.” to align with the other questions.

Final Summary Question:

The same:

How should optimal metabolic control both clinically and biochemically (like lactate, ketones and/or lipids) be achieved in liver Glycogen Storage Disease?

Code: G4Hypo1
What can be done to prevent hypoglycemia or restore blood sugar to a safe level in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("hypoglycemia"[tiab]) AND ("prevention"[tiab] OR "restore"[tiab])

Found articles:
1. Prevention of complications in glycogen storage disease type Ia with optimization of metabolic control. Dambska M, Labrador EB, Kuo CL, Weinstein DA. Pediatr Diabetes. 2017 Aug;18(5):327-331. doi: 10.1111/pedi.12540. Epub 2017 Jun 1. Review. PMID: 28568353.

2. Optimal daytime feeding regimen to prevent postprandial hypoglycemia in type 1 glycogen storage disease. Wolfsdorf JI, Ehrlich S, Landy HS, Crigler JF Jr. Am J Clin Nutr. 1992 Sep;56(3):587-92. PMID: 150307.

3. Safety issues associated with dietary management in patients with hepatic glycogen storage disease. Steunenberg TAH, Peeks F, Hoogeveen IJ, Mitchell JJ, Mundy H, de Boer F, Lubout CMA, de Souza CF, Weinstein DA, Derks TGJ. Mol Genet Metab. 2018 Sep;125(1-2):79-85. doi: 10.1016/j.ymgme.2018.07.004. Epub 2018 Jul 18. PMID: 30037503

Conclusion of articles:
1. Dietary treatment with gastric dripfeeding and/or complex carbohydrates is the cornerstone for prevention of hypoglycaemia.
2. There are safety issues associated with dietary management that is used to prevent hypoglycaemia. Several safety measures are mentioned, but these are not addressed in a prospective manner. Furthermore, there is a necessity for a more non-invasive manner to detect and prevent hypoglycaemia.

Summary Question answered:
No.

Final Summary Question:

The same:

What can be done to prevent hypoglycemia or restore blood sugar to a safe level in patients

with liver Glycogen Storage Disease?

Code: G4Hypo2
What are the acute and chronic consequences of hypoglycemia in patients with liver Glycogen Storage Disease?

Search Strategy
Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("hypoglycemia"[tiab]) AND ("complication*"[tiab])

Found articles:
1. Prevention of complications in glycogen storage disease type Ia with optimization of metabolic control. Dambska M, Labrador EB, Kuo CL, Weinstein DA. Pediatr Diabetes. 2017 Aug;18(5):327-331. doi: 10.1111/pedi.12540. Epub 2017 Jun 1. Review. PMID: 28568353

2. The effect of tailoring of cornstarch intake on stature in children with glycogen storage disease type III. El-Karaksy H, El-Raziky MS, Anwar G, Mogahed E. J Pediatr Endocrinol Metab. 2015 Jan;28(1-2):195-200. doi: 10.1515/jpem-2014-0145. PMID: 25153581

Conclusion of articles:
1. Much is known and described about the acute consequences of hypoglycaemia in liver GSD. But symptoms of acute hypoglycaemia have not been described systematically such as in diabetes.
2. There are many uncertainties on the chronic consequences. Although many associations have been mentioned, mechanisms are not fully identified.
3. Among patients there is evidence that there is hypoglycaemia unawareness from patients and parents that have difficulty detecting hypoglycaemia episodes.

Summary Question answered:
Partly, there are many studies of the complications of hypoglycemia, but none have systematically identified symptoms of hypoglycemia.

Final Summary Question:

The same:

What are the acute and chronic consequences of hypoglycemia in patients with liver Glycogen Storage Disease?

Code: G4CGM1

What is the role of continuous glucose monitoring in patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND "continuous glucose monitoring"[tiab]

Found articles:

1. Continuous glucose monitoring in children with glycogen storage disease type I.

Kasapkara ÇS, Cinasal Demir G, Hasanoğlu A, Tümer L. Eur J Clin Nutr. 2014 Jan;68(1):101-5. doi: 10.1038/ejcn.2013.186. Epub 2013 Oct 23. PMID: 24149443.

2. Continuous glucose monitoring in the treatment of obesity in patients with glycogen storage disease type Ia. Korljan Jelaska B, Ostojić SB, Berović N, Kokić V. Endocrinol Diabetes Metab Case Rep. 2013;2013:130056. doi: 10.1530/EDM-13-0056. Epub 2013 Dec 1. PMID: 24683476

3. The use of continuous glucose monitoring in the practical management of glycogen storage disorders. White FJ, Jones SA. J Inherit Metab Dis. 2011 Jun;34(3):631-42. doi: 10.1007/s10545-011-9335-3. Epub 2011 May 10. PMID: 21556835

4. Continuous glucose monitoring in conditions other than diabetes. Maran A, Crepaldi C, Avogaro A, Catuogno S, Burlina A, Poscia A, Tiengo A. Diabetes Metab Res Rev. 2004 Nov-Dec;20 Suppl 2:S50-5. PMID: 15551341.

5. Continuous glucose monitoring in children with glycogen storage disease type I.

Hershkovitz E, Rachmel A, Ben-Zaken H, Phillip M. J Inherit Metab Dis. 2001 Dec;24(8):863-9. PMID: 11916320.

6. A case of perioperative glucose control by using an artificial pancreas in a patient with glycogen storage disease. Yatabe T, Nakamura R, Kitagawa H, Munekage M, Hanazaki K. J Artif Organs. 2016 Mar;19(1):100-3. doi: 10.1007/s10047-015-0855-8. Epub 2015 Jul 21. PMID: 26194122

7. A preliminary study of telemedicine for patients with hepatic glycogen storage disease and their healthcare providers: from bedside to home site monitoring.

Hoogeveen IJ, Peeks F, de Boer F, Lubout CMA, de Koning TJ, Te Boekhorst S, Zandvoort RJ, Burghard R, van Spronsen FJ, Derks TGJ. J Inherit Metab Dis. 2018 Mar 29. doi: 10.1007/s10545-018-0167-2. [Epub ahead of print] PMID: 29600495.

8. Role of continuous glucose monitoring in the management of glycogen storage disorders. Herbert M, et al. PMID: 29802555

Conclusion of articles:

1. Continuous glucose monitoring has been used in liver GSD for prevention and monitoring of glycemia, perioperative care and for specific patient questions (such as first school day).
2. There is a suggestion of incorporating CGM data for big data analysis for a better understanding of the individual patient and metabolic control.
3. The CGMS was found to be a safe, effective, and reliable method for optimizing treatment in patients with GSD I, III, and IX.
4. There has been discussion in literature on the accuracy of CGM in comparison with other methods. This should be examined more systematically, especially for very low glucose levels.

Summary Question answered:

Partly, but there are many options for research left.

Final Summary Question:

The same:

What is the role of continuous glucose monitoring in patients with liver Glycogen Storage Disease?

Code: G4GM1

How can the accuracy of glucose monitoring be improved to better control glucose and prevent hypoglycemia for patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“glucose monitoring”[tiab] OR "accuracy"[tiab])

Found articles:

See G4CGM1

Conclusion of articles:

1. There has been discussion in literature on the accuracy of CGM in comparison with other methods. This should be examined more systematically, especially for very low glucose levels.

Summary Question answered:

No.

Final Summary Question:

The same:

How can the accuracy of glucose monitoring be improved to better control glucose and prevent hypoglycemia for patients with liver Glycogen Storage Disease?

Code: G4LH1

How do body changes throughout life impact blood sugars in patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“euglycemia”[tiab] OR "normoglycemia"[tiab] OR "hypoglycemia"[tiab]) AND ("Child"[tiab] OR “Adult"[tiab] OR “Ageing”[tiab])

Found articles:

1. Diabetes mellitus in a patient with glycogen storage disease type Ia: a case report.

Cohn A, Ohri A. J Med Case Rep. 2017 Nov 12;11(1):319. doi: 10.1186/s13256-017-1462-5. PMID: 29127952.

2. Dietary management in glycogen storage disease type III: what is the evidence?

Derks TG, Smit GP. J Inherit Metab Dis. 2015 May;38(3):545-50. doi: 10.1007/s10545-014-9756-x. Epub 2014 Aug 28. Review. PMID: 25164784

3. The effect of tailoring of cornstarch intake on stature in children with glycogen storage disease type III. El-Karaksy H, El-Raziky MS, Anwar G, Mogahed E. J Pediatr Endocrinol Metab. 2015 Jan;28(1-2):195-200. doi: 10.1515/jpem-2014-0145.

PMID: 25153581.

4. Glycogen storage diseases. Phenotypic, genetic, and biochemical characteristics, and therapy. Wolfsdorf JI, Holm IA, Weinstein DA. Endocrinol Metab Clin North Am. 1999 Dec;28(4):801-23. Review. PMID: 10609121.

5. Late presentation of glycogen storage disease types Ia and III in children with short stature and hepatomegaly. Quackenbush D, Devito J, Garibaldi L, Buryk M.

J Pediatr Endocrinol Metab. 2018 Mar 28;31(4):473-478. doi: 10.1515/jpem-2017-0209. PMID: 29374762.

6. Safety issues associated with dietary management in patients with hepatic glycogen storage disease. Steunenberg TAH, Peeks F, Hoogeveen IJ, Mitchell JJ, Mundy H, de Boer F, Lubout CMA, de Souza CF, Weinstein DA, Derks TGJ. Mol Genet Metab. 2018 Sep;125(1-2):79-85. doi: 10.1016/j.ymgme.2018.07.004. Epub 2018 Jul 18. PMID: 30037503

7. Endogenous glucose production from infancy to adulthood: a non-linear regression model. Huidekoper HH, Ackermans MT, Ruiter AF, Sauerwein HP, Wijburg FA. Arch Dis Child. 2014 Dec;99(12):1098-102. doi: 10.1136/archdischild-2013-305718. Epub 2014 Jul 4. PMID: 24996789

Conclusion of articles:

1. From studies into metabolism in healthy adults, it is known that endogenous glucose production is dependent on weight, height and age.
2. There is evidence from case series that older GSD patients are less prone to having

episodes of hypoglycemia.

Summary Question answered:
Partly, for the healthy population this is answered, but not for the liver GSD population.

Final Summary Question:

The same:

How do body changes throughout life impact blood sugars in patients with liver Glycogen Storage Disease?

Code: G4EM1

How should sickness and emergency situations be managed for patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“Emergency”[tiab] OR “sick*”[tiab] OR “safety”[tiab])

Found articles:

1. A preliminary study of telemedicine for patients with hepatic glycogen storage disease and their healthcare providers: from bedside to home site monitoring.

Hoogeveen IJ, Peeks F, de Boer F, Lubout CMA, de Koning TJ, Te Boekhorst S, Zandvoort RJ, Burghard R, van Spronsen FJ, Derks TGJ. J Inherit Metab Dis. 2018 Mar 29. doi: 10.1007/s10545-018-0167-2. [Epub ahead of print] PMID: 29600495.

2. Safety issues associated with dietary management in patients with hepatic glycogen storage disease. Steunenberg TAH, Peeks F, Hoogeveen IJ, Mitchell JJ, Mundy H, de Boer F, Lubout CMA, de Souza CF, Weinstein DA, Derks TGJ. Mol Genet Metab. 2018 Sep;125(1-2):79-85. doi: 10.1016/j.ymgme.2018.07.004. Epub 2018 Jul 18. PMID: 30037503

Conclusion of articles:

1. According to the guidelines and expert opinions, there are several manners in which emergency situations are managed. However, this is not systematically studied and there is no global consensus.

Summary Question answered:

No.

Final Summary Question:

The same:

How should sickness and emergency situations be managed for patients with liver Glycogen Storage Disease?

Code: G4ERGT1

What are the best options for achieving sufficient amount of working enzyme in patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“Enzyme activity”[tiab]) AND "Therapy"[tiab]

Found articles:

See G4GTR

1. Sustained hepatic and renal glucose-6-phosphatase expression corrects glycogen storage disease type Ia in mice. Sun MS, Pan CJ, Shieh JJ, Ghosh A, Chen LY, Mansfield BC, Ward JM, Byrne BJ, Chou JY. Hum Mol Genet. 2002 Sep 1;11(18):2155-64. PMID: 12189168
2. Preclinical Development of New Therapy for Glycogen Storage Diseases. Sun B, Brooks ED, Koeberl DD. Curr Gene Ther. 2015;15(4):338-47. Review. PMID: 26122079

Conclusion of articles:

1. There are no suggestions of enzyme replacement therapy in liver GSD, only in GSD II (Pompe).
2. There is much research that indicates that gene therapy could restore working enzyme activity.

Summary Question answered:

No. I recommend that we add for clarity that we are talking about gene therapy and enzyme replacement therapy for example**.**

Final Summary Question:

Changed:

What are the best options (for example gene therapy or enzyme replacement therapy) for achieving sufficient amount of working enzyme in patients with liver Glycogen Storage Disease?

Code: G4GTR1

What are the risks of gene therapy for patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“Gene therapy”[Mesh] OR “Gene therapy”[tiab])

Found articles:

1. Preclinical Development of New Therapy for Glycogen Storage Diseases. Sun B, Brooks ED, Koeberl DD. Curr Gene Ther. 2015;15(4):338-47. Review. PMID: 26122079.
2. Liver-directed gene therapy for murine glycogen storage disease type Ib. Kwon JH, Lee YM, Cho JH, Kim GY, Anduaga J, Starost MF, Mansfield BC, Chou JY. Hum Mol Genet. 2017 Nov 15;26(22):4395-4405. doi: 10.1093/hmg/ddx325. PMID: 28973635.
3. Glycogen storage disease type Ia mice with less than 2% of normal hepatic glucose-6-phosphatase-α activity restored are at risk of developing hepatic tumors. Kim GY, Lee YM, Kwon JH, Cho JH, Pan CJ, Starost MF, Mansfield BC, Chou JY.

Mol Genet Metab. 2017 Mar;120(3):229-234. doi: 10.1016/j.ymgme.2017.01.003. Epub 2017 Jan 10. PMID: 28096054.
4. Systemic Correction of Murine Glycogen Storage Disease Type IV by an AAV-Mediated Gene Therapy. Yi H, Zhang Q, Brooks ED, Yang C, Thurberg BL, Kishnani PS, Sun B. Hum Gene Ther. 2017 Mar;28(3):286-294. doi: 10.1089/hum.2016.099. Epub 2016 Nov 10. PMID: 27832700.
5. Adeno-associated virus gene therapy prevents hepatocellular adenoma in murine model of glycogen storage disease type Ia. Wang L. Hepatology. 2012 Nov;56(5):1593-5. doi: 10.1002/hep.25894. No abstract available. PMID: 22706804.
6. Hepatic lentiviral gene transfer prevents the long-term onset of hepatic tumours of glycogen storage disease type 1a in mice. Clar J, Mutel E, Gri B, Creneguy A, Stefanutti A, Gaillard S, Ferry N, Beuf O, Mithieux G, Nguyen TH, Rajas F. Hum Mol Genet. 2015 Apr 15;24(8):2287-96. doi: 10.1093/hmg/ddu746. Epub 2015 Jan 5.

PMID: 25561689.
7. Downregulation of pathways implicated in liver inflammation and tumorigenesis of glycogen storage disease type Ia mice receiving gene therapy. Kim GY, Kwon JH, Cho JH, Zhang L, Mansfield BC, Chou JY. Hum Mol Genet. 2017 May 15;26(10):1890-1899. doi: 10.1093/hmg/ddx097. PMID: 28334808.
8. In search of proof-of-concept: gene therapy for glycogen storage disease type Ia.

Koeberl DD. J Inherit Metab Dis. 2012 Jul;35(4):671-8. doi: 10.1007/s10545-012-9454-5. Epub 2012 Feb 7. PMID: 22310927.
9. Pathogenesis of growth failure and partial reversal with gene therapy in murine and canine Glycogen Storage Disease type Ia. Brooks ED, Little D, Arumugam R, Sun B, Curtis S, Demaster A, Maranzano M, Jackson MW, Kishnani P, Freemark MS, Koeberl DD. Mol Genet Metab. 2013 Jun;109(2):161-70. doi: 10.1016/j.ymgme.2013.03.018. Epub 2013 Apr 6. PMID: 23623482.

10. Prevention of hepatocellular adenoma and correction of metabolic abnormalities in murine glycogen storage disease type Ia by gene therapy. Lee YM, Jun HS, Pan CJ, Lin SR, Wilson LH, Mansfield BC, Chou JY. Hepatology. 2012 Nov;56(5):1719-29. doi: 10.1002/hep.25717. Epub 2012 Aug 27. PMID: 22422504.
11. Recent development and gene therapy for glycogen storage disease type Ia.

Chou JY, Kim GY, Cho JH. Liver Res. 2017 Sep;1(3):174-180. doi: 10.1016/j.livres.2017.12.001. PMID: 29576889
12. Complete normalization of hepatic G6PC deficiency in murine glycogen storage disease type Ia using gene therapy. Yiu WH, Lee YM, Peng WT, Pan CJ, Mead PA, Mansfield BC, Chou JY. Mol Ther. 2010 Jun;18(6):1076-84. doi: 10.1038/mt.2010.64. Epub 2010 Apr 13. PMID: 20389290.
13. Adenovirus-mediated gene therapy in a mouse model of glycogen storage disease type 1a. Chou JY, Zingone A, Pan CJ. Eur J Pediatr. 2002 Oct;161 Suppl 1:S56-61. Epub 2002 Jul 19. Review. PMID: 12373573.

14. Sustained hepatic and renal glucose-6-phosphatase expression corrects glycogen storage disease type Ia in mice. Sun MS, Pan CJ, Shieh JJ, Ghosh A, Chen LY, Mansfield BC, Ward JM, Byrne BJ, Chou JY. Hum Mol Genet. 2002 Sep 1;11(18):2155-64. PMID: 12189168.
15. Long-term efficacy following readministration of an adeno-associated virus vector in dogs with glycogen storage disease type Ia.Demaster A, Luo X, Curtis S, Williams KD, Landau DJ, Drake EJ, Kozink DM, Bird A, Crane B, Sun F, Pinto CR, Brown TT, Kemper AR, Koeberl DD. Hum Gene Ther. 2012 Apr;23(4):407-18. doi: 10.1089/hum.2011.106. Epub 2012 Mar 8. PMID: 22185325.
16. Neonatal gene therapy of glycogen storage disease type Ia using a feline immunodeficiency virus-based vector. Grinshpun A, Condiotti R, Waddington SN, Peer M, Zeig E, Peretz S, Simerzin A, Chou J, Pann CJ, Giladi H, Galun E. Mol Ther. 2010 Sep;18(9):1592-8. doi: 10.1038/mt.2010.119. Epub 2010 Jun 22. PMID: 20571544
17. Rescue of GSDIII Phenotype with Gene Transfer Requires Liver- and Muscle-Targeted GDE Expression. Vidal P, Pagliarani S, Colella P, Costa Verdera H, Jauze L, Gjorgjieva M, Puzzo F, Marmier S, Collaud F, Simon Sola M, Charles S, Lucchiari S, van Wittenberghe L, Vignaud A, Gjata B, Richard I, Laforet P, Malfatti E, Mithieux G, Rajas F, Comi GP, Ronzitti G, Mingozzi F. Mol Ther. 2018 Mar 7;26(3):890-901. doi: 10.1016/j.ymthe.2017.12.019. Epub 2017 Dec 28. PMID: 29396266
18. Long-term safety and efficacy of AAV gene therapy in the canine model of glycogen storage disease type Ia. Lee YM, Conlon TJ, Specht A, Coleman KE, Brown LM, Estrella AM, Dambska M, Dahlberg KR, Weinstein DA. J Inherit Metab Dis. 2018 May 25. doi: 10.1007/s10545-018-0199-7. [Epub ahead of print]

PMID: 29802554
19. Adeno-associated virus-mediated correction of a canine model of glycogen storage disease type Ia. Weinstein DA, Correia CE, Conlon T, Specht A, Verstegen J, Onclin-Verstegen K, Campbell-Thompson M, Dhaliwal G, Mirian L, Cossette H, Falk DJ, Germain S, Clement N, Porvasnik S, Fiske L, Struck M, Ramirez HE, Jordan J, Andrutis K, Chou JY, Byrne BJ, Mah CS. Hum Gene Ther. 2010 Jul;21(7):903-10. doi: 10.1089/hum.2009.157.

PMID: 20163245

Conclusion of articles:

1. rAAV-GPE-hG6PC treatment in GSD-Ia dogs was found to be safe and efficacious in short and long-term. Studies in humans are being performed.

2. There is debate on the amount of enzyme level required to prevent complications from occurring.

Summary Question answered:

Partly. Studies in humans have to be continued. I would recommend that we change the question to “risks and benefits” to be more inclusive for the gene therapy concept as a whole.

Final Summary Question:

Changed:

What are the risks and benefits of gene therapy for patients with liver Glycogen Storage Disease?

Code: G4Guide1

Can consensus guidelines (for management) be achieved for patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“Guidelines”[tiab] OR “Consensus”[tiab])

Found articles:

Conclusion of articles:

1. Although there are guidelines, a global consensus has not been reached to treat individual patients. More longitudinal follow-up data from international cohorts is necessary to take into account social, environmental and patient characteristics.

Summary Question answered:

No.

Final Summary Question:

The same:

Can consensus guidelines (for management) be achieved for patients with liver Glycogen Storage Disease?

Code: G4OCD1

What are the side effects of over the counter drugs for patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND "Nonprescription Drugs"[Mesh]

Found articles:

None.

Conclusion of articles:

1. There has not been research on side effects of over the counter drugs.

Summary Question answered:

No.

Final Summary Question:

The same:

What are the side effects of over the counter drugs for patients with liver Glycogen Storage Disease?

Code: G4Sleep1

What is the impact of disrupted sleep in patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:

Found articles:

See G3DT2

Conclusion of articles:

I propose we merge this question with G3DT2 since that question incorporates disrupted sleep.

Summary Question answered:

No.

Final Summary Question:

None.

Code: G4Safe1

How can we maximize safety during the overnight period for patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed:

Found articles:

See G4Night1

Conclusion of articles:

Since this question will compete with G4Night1, I recommend merging these two questions. See G4Night1. Furthermore G4Safe1 will be added to G4Night1.

Summary Question answered:

No.

Final Summary Question:

See G4Night1

Code: G4Night1

What are the different options for overnight treatment for patients with liver Glycogen Storage Disease and what are the risks and benefits of each option?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“Overnight”[tiab] OR “Nocturnal”[tiab] OR “Night”[tiab]) AND “Treatment”[tiab].

Found articles:

1. Dietary treatment of glycogen storage disease type Ia: uncooked cornstarch and/or continuous nocturnal gastric drip-feeding? Derks TG, Martens DH, Sentner CP, van Rijn M, de Boer F, Smit GP, van Spronsen FJ. Mol Genet Metab. 2013 May;109(1):1-2. doi: 10.1016/j.ymgme.2013.02.005. Epub 2013 Feb 15. No abstract available.

PMID: 23480859

2. Safety and Efficacy of Chronic Extended Release Cornstarch Therapy for Glycogen Storage Disease Type I. Ross KM, Brown LM, Corrado MM, Chengsupanimit T, Curry LM, Ferrecchia IA, Porras LY, Mathew JT, Weinstein DA. JIMD Rep. 2016;26:85-90. doi: 10.1007/8904_2015_488. Epub 2015 Aug 25.

PMID: 26303612

3. Safety issues associated with dietary management in patients with hepatic glycogen storage disease. Steunenberg TAH, Peeks F, Hoogeveen IJ, Mitchell JJ, Mundy H, de Boer F, Lubout CMA, de Souza CF, Weinstein DA, Derks TGJ. Mol Genet Metab. 2018 Sep;125(1-2):79-85. doi: 10.1016/j.ymgme.2018.07.004. Epub 2018 Jul 18. PMID: 30037503.

Conclusion of articles:

1. There are many articles referenced to in the guidelines that described the use of (extended release) cornstarch and nocturnal gastric dripfeeding.
2. Safety issues with (nocturnal) dietary management have been described, but no prospective study has been performed to assess manners in which safety overnight can be ensured.

Summary Question answered:

No. As recommended earlier, we can merge this question with G4Safe1.

Final Summary Question:

Merged:

What are the risks and benefits of different options for overnight treatment for patients with liver Glycogen Storage Disease and how can we maximize safety?

Code: G4Pers1

Is there a role for personalized treatment for patients with liver Glycogen Storage Disease?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND ("Precision Medicine"[tiab] OR "Personalized"[tiab]).

Found articles:

1. Clinical and biochemical heterogeneity between patients with glycogen storage disease type IA: the added value of CUSUM for metabolic control. Peeks F, Steunenberg TAH, de Boer F, Rubio-Gozalbo ME, Williams M, Burghard R, Rajas F, Oosterveer MH, Weinstein DA, Derks TGJ. J Inherit Metab Dis. 2017 Sep;40(5):695-702. doi: 10.1007/s10545-017-0039-1. Epub 2017 Apr 10. PMID: 28397058

Conclusion of articles:

1. The guidelines give general treatment guidelines. The abovementioned study identified external and internal differences between GSD Ia patients that encourage personalized treatment.

Summary Question answered:

No. I recommend we rephrase this question to how we can personalize treatment.

Final Summary Question:

Changed:

How can we personalize treatment for patients with liver Glycogen Storage Disease?

Code: G4Weight1

How can patients with liver Glycogen Storage Disease achieve and/or maintain a healthy weight throughout life?

Search Strategy

Guidelines: Genereviews for all liver GSD types, ESGSDI, ISGSDIII.

Pubmed: ("Glycogen Storage Disease"[Mesh] OR "Glycogen Storage Disease"[tiab]) AND (“Weight”[tiab] OR “Obesity”[tiab] OR “overweight[tiab]).

Found articles:

1. The health impact of nighttime eating: old and new perspectives. Kinsey AW, Ormsbee MJ. Nutrients. 2015 Apr 9;7(4):2648-62. doi: 10.3390/nu7042648. Review.

PMID: 25859885.

2. Glycogen storage disease type I: clinical and laboratory profile. Santos BL, Souza CF, Schuler-Faccini L, Refosco L, Epifanio M, Nalin T, Vieira SM, Schwartz IV. J Pediatr (Rio J). 2014 Nov-Dec;90(6):572-9. doi: 10.1016/j.jped.2014.02.005. Epub 2014 Jul 11. PMID: 25019649

3. Glycogen storage disease type III presenting with secondary diabetes and managed with insulin: a case report. Ismail H. Cases J. 2009 Jun 17;2:6891. doi: 10.4076/1757-1627-2-6891. PMID: 19829878.

4. Continuous glucose monitoring in the treatment of obesity in patients with glycogen storage disease type Ia. Korljan Jelaska B, Ostojić SB, Berović N, Kokić V. Endocrinol Diabetes Metab Case Rep. 2013;2013:130056. doi: 10.1530/EDM-13-0056. Epub 2013 Dec 1. PMID: 24683476.

5. Bariatric surgery is not contraindicated in obese patients suffering from glycogen storage disease type IXa. A case report with follow-up at three years. Musella M, Milone M, Maietta P, Bianco P, Pisapia A, Gaudioso D, Palumbo R. Int J Surg Case Rep. 2014;5(10):686-8. doi: 10.1016/j.ijscr.2014.06.009. Epub 2014 Aug 15.

PMID: 25194605

6. Obesity and reversed growth retardation in a child with type Ia glycogen storage disease. Karnsakul W, Gillespie S, Skitarelic K, Hummel M. J Pediatr Endocrinol Metab. 2010 May;23(5):507-12. PMID: 20662351

7. Prevention of complications in glycogen storage disease type Ia with optimization of metabolic control. Dambska M, Labrador EB, Kuo CL, Weinstein DA. Pediatr Diabetes. 2017 Aug;18(5):327-331. doi: 10.1111/pedi.12540. Epub 2017 Jun 1. Review. PMID: 28568353

8. Clinical and biochemical heterogeneity between patients with glycogen storage disease type IA: the added value of CUSUM for metabolic control. Peeks F, Steunenberg TAH, de Boer F, Rubio-Gozalbo ME, Williams M, Burghard R, Rajas F, Oosterveer MH, Weinstein DA, Derks TGJ. J Inherit Metab Dis. 2017 Sep;40(5):695-702. doi: 10.1007/s10545-017-0039-1. Epub 2017 Apr 10. PMID: 28397058

Conclusion of articles:

1. Obesity is associated with liver GSD and cornstarch/dripfeeding treatment.
2. Health risks such as metabolic syndrome, diabetes mellitus, and cardiovascular events have been described in liver GSD.
3. Tools such as continuous glucose monitoring, but also bariatric surgery have been mentioned as a tool to treat obesity.
3. Optimizing and personalizing dietary treatment for patients with liver GSD suggests better metabolic control with prevention of overtreatment and therefore obesity. Although prevention of overtreatment can be difficult in patients that are difficult to regulate with dietary treatment.

Summary Question answered:

No. As discussed earlier, we can merge this question with G1Com1n.

Final Summary Question:

How can patients with liver Glycogen Storage Disease achieve and/or maintain a healthy weight throughout life?