

Anaesthesia recommendations for patients suffering from

Glycogen Storage Disease Type I

Disease name: Glycogen storage disease type I

ICD 10: E74.0

Synonyms: von Gierke disease, Glycogenosis type I, Glucose-6-phosphatase deficiency, GSD-I

Disease summary: Glycogen storage disease type I is a rare autosomal recessive inherited disorder with an annual incidence of approximately 1/100.000 [1]. Due to a deficiency of glucose-6-phosphatase [2], glycogen stored in the liver cannot be metabolized. This leads to poor tolerance to fasting and increased risk of hypoglycemia and lactate acidosis. The accumulation of glycogen [3] in liver tissue leads to hepatomegaly and later in life to an increased risk of hepatocellular adenoma and/or carcinoma. The clinical presentation is accompanied by growth retardation. Renal affection, hyperlipidemia [4] and platelet dysfunctions [5] are common. Perioperative management has to focus on metabolic homeostasis by adequate glucose supply and prevention of lactate acidosis exacerbation. Platelet dysfunction poses a challenge to regional anesthesia techniques and hemostasis throughout an operation. Subtype Ib is caused by deficiency of glucose-6-phosphatase-translocase and is accompanied by neutrophil dysfunction, recurrent infections, autoimmune thyroid disease and inflammatory bowel disease.

Medicine in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong



Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Typical surgery

Oral / facial surgery in type Ib: Relapsing aphthous gingivostomatitis and its complications

Abdominal surgery: adenoma and carcinoma resection [6,7], liver transplantation, liver biopsy, pancreatitis

Type of anesthesia

General anaesthesia as well as all regional anaesthesia techniques have been performed in patients with GSD-I. Both demonstrate specific issues in GSD-I that the anaesthesiologist has to be aware of.

General anaesthesia: Prolonged fasting in the perioperative period leads to hypoglycemia and lactate acidosis. Adequate glucose supply throughout the fasting period is essential for homeostasis of the metabolic situation [8,9]. Hepatomegaly and enzyme induction can potentially lead to altered pharmacology of anaesthetic drugs, both in reduced or accelerated clearance, although this has not been studied specifically.

Regional anaesthesia: GSD-I is associated with platelet dysfunction [5,10], which is in part correlated to the extent of the dyslipidemia [4]. Clinically, the platelet dysfunction can lead to recurrent epistaxis and ecchymosis, which should be noted as important sign for later hemorrhagic adverse events throughout an operation. Platelet count and functional testing can quantify the extent of the platelet dysfunction prior to planned surgery. Neuraxial anaesthesia, specifically epidural catheters have been placed without complications [6]. In several cases, specifically for caesarean sections, spinal anaesthesia has been performed safely [11].

Necessary additional diagnostic procedures (preoperative)

Prior to planned surgery, the following blood tests should be performed: Complete blood count (neutrophil count in subtype GSD-Ib), creatinine, triglyceride, cholesterol [4], electrolyte status, uric acid [12], urine status [13], thyroid hormone status [14], and if possible platelet function.

Lactate and blood glucose levels have to be monitored closely during the fasting period until the regular enteral glucose supply is re-established.

Echocardiography and ECG can be helpful when signs of pulmonary hypertension, a rare but severe complication described in GSD-I are present [15,16].

Patients should wear a medical alert identification. Admission to the hospital should be 24 hours prior to planned surgery to allow for adequate infusion therapy and metabolic control [17].

Particular preparation for airway management

In GSD-Ib, oral aphthous gingivostomatitis is common. Its complications could potentially lead to problems in airway management, but airway problems have not been reported specifically so far.

Particular preparation for transfusion or administration of blood products

Platelet dysfunction can be treated by transfusion of homologue platelet concentrates. Nonsteroidal anti-inflammatory drugs and medications that affect platelet function should be avoided. In case of severe neutrophil dysfunction in GSD-Ib, hematopoietic stem cell transplantation can be an option and transfusion management should in this case be directed in order to avoid later incompatibilities. Otherwise, GSD-I does not pose specific problems for transfusions of RBCs or plasma. There is no data on the – theoretically evident – benefit of desmopressin.

Particular preparation for anticoagulation

Not reported. Although arterial dysfunction, characterized by increased media thickness, is described, the overall risk of atherosclerosis and cardiovascular complications does not seem to be increased in early adulthood [18,19].

Particular precautions for positioning, transport or mobilisation

GSD-I can lead to osteopenia and osteoporosis, although they are usually not associated with fractures. Given the case, careful positioning is advised.

Due to hepatomegaly, abdominal compression in prone position should be avoided or minimized in order to avoid hepatic injuries due to compression.

Probable interaction between anesthetic agents and patient's long term medication

Common drugs used in long-term therapy are ACE-Inhibitors and allopurinole. Hepatomegaly can be associated with enzyme induction and can potentially lead to accelerated or reduced hepatic clearance.

Anaesthesiologic procedure

Glucose supply and perioperative fasting:

Standard therapy for the reduced fasting tolerance in GSD-I is enteral supplementation with cornstarch [20]. Continuous supply of glucose is warranted by delayed resorption of long-chained carbohydrates, which are delivered enterally by nasogastral tube feeding overnight[9]. In infancy, nasogastral feeding is performed as continuous feeding, later as intermittent feeding every 4 to 6 hours [21]. During the obligatory preoperative fasting period prior to planned surgery, glucose uptake must be switched to parenteral glucose infusion. The amount of glucose delivered can vary individually and has to be adapted based on the dosage used in long-term therapy for this specific patient [22]. For orientation, 0.5-0.6g/kg/h in infancy and 0.3-0.4g/kg/h for the older child seem to fit most patients [10]. Table 1 shows practicable dosage regimes.

		child	infant	neonate
requirement	g/kg/h	0.3 – 0.4	0.5	0.6
	mg/kg/min	5.0 – 6.7	8.3	10.0

enteral	cornstarch g/kg every 4h	1.2 – 1.6	2.0	2.4
	cornstarch g/kg every 6h	1.8 – 2.4		

parenteral	G-5% in ml/kg/h	6.0 – 8.0	10.0	12.0
	G-10% in ml/kg/h	3 - 4	5	6
	G-12.5% in ml/kg/h	2.4 – 3.2	4	4.8
	G-17.5% in ml/kg/h	1.71 – 2.29	2.86	3.43
	G-20% in ml/kg/h	1.5 - 2	2.5	3

Table 1: glucose requirements in different age groups

For an infusion, a standardized Ringer-acetate solution with additional glucose can be used. [8]. The infusion should be free of lactate and the glucose should be concentrated as high as possible in order to avoid excess volume and lactate[6]. Table 2 demonstrates possible infusions. For use in peripheral veins, only solutions containing less than 12.5% glucose should be used.

	desired overall glucose concentration	using ringer-acetate's solution	using E148G1Paed
additional G40%	10%	375ml ringer-acetate + 125ml G40%	385ml E148G1Paed + 115ml G40%
	12.5%	345ml ringer-acetate + 155ml G40%	355ml E148G1Paed + 145ml G40%
	17.5%	280ml ringer-acetate + 220ml G40%	290ml E148G1Paed + 210ml G40%
additional G70%	10%	430ml ringer-acetate	435ml E148G1Paed +

		+ 70ml G70%	65ml G70%
	12.5%	410ml ringer-acetate + 90ml G70%	420ml E148G1Paed + 80ml G70%
	17.5%	375ml ringer-acetate + 125ml G70%	380ml E148G1Paed + 120ml G70%

Table 2: possible infusions

During parenteral substitution, blood glucose levels and lactate have to be monitored closely. Repeated measurements should be performed throughout the fasting period until oral cornstarch feeding is re-established. Aim for Glucose levels > 70mg/dl and avoid rapid glucose fluxes.

Different from other glycogen-storage-diseases like type III or type V, GSD-I does not involve skeletal muscle cell and does not demonstrate signs of a myopathy [3]. GSD-I is not associated with mutations of the RYR-receptor [23], therefore not resulting in limitations for inhalative anesthetics. There are case reports of an increased risk for rhabdomyolysis in GSD-I patients [24]. A restrictive use of suxamethonium, only in situations where it is explicitly needed, seems to be reasonable.

The associated neutrophil defect of phagocytosis in GSD subtype Ib leads to an increased risk of infections. Asepsis is obligatory for all invasive procedures. A perioperative antibiotic therapy should cover staphylococcus [25].

Particular or additional monitoring

Unreliable BIS-monitoring in GSD-I has been reported [26]. In the specific case, hypoglycemia led to lower BIS levels and masked insufficient anesthesia depth. Providers should be aware of possible confounders, such as hypoglycemia, when applying BIS-monitoring or other techniques.

Placement of invasive arterial catheters is suggested by many authors for frequent drawing of blood samples.

Possible complications

Maintaining metabolic homeostasis should be the primary target in order to avoid possible complications. Lactate acidosis can occur. A calculated sodium bicarbonate supplementation can be used for correction of acidosis [8, 27]. Controlled hyperventilation is not suggested, as it may lead to increased mobilization of lactate from muscle tissue, which cannot be metabolized when present in excess.

Postoperative care

Blood gas analysis, lactate, and blood glucose levels have to be measured repeatedly until 4 hours after re-establishment of oral feeding.

Information about emergency-like situations / Differential diagnostics

Seizures caused by hypoglycemia can occur. If signs of cerebral seizures are present, immediate measurement of blood gases and blood glucose level has to be performed. Seizure therapy, aside from giving additional glucose, is not different.

Ambulatory anesthesia

In order to warrant continuous glucose supply and metabolic monitoring, ambulatory anesthesia is not suggested.

Obstetrical anesthesia

As patients with GSD-I have a normal fertility, pregnancies are possible and described[28]. A prenatal diagnosis is possible. For delivery, caesarian sections[11] and vaginal delivery is possible[29].

Literature and internet links

1. Froissart R, Piraud M, Boudjemline A, et al (2011) Glucose-6-phosphatase deficiency. *Orphanet J Rare Dis* 6(1):27.doi:10.1186/1750-1172-6-27
2. van Schaftingen E, Gerin I (2002) The glucose-6-phosphatase system. *The Biochemical journal* 362(Pt 3):513–532
3. Bali DS, Chen YT, Goldstein JL. (2006) Glycogen Storage Disease Type I. *GeneReviews*
4. Bandsma, Robert H J, Smit, G Peter A, Kuipers F (2002) Disturbed lipid metabolism in glycogen storage disease type 1. *European journal of pediatrics* 161 Suppl 1:S65-9. doi: 10.1007/s00431-002-1007-8
5. Ambruso DR, McCabe ER, Anderson D, et al (1985) Infectious and bleeding complications in patients with glycogenosis Ib. *American journal of diseases of children* (1960)139(7):691–697
6. Ogawa M, Shimokohjin T, Seto T, et al (1995) Anesthesia for hepatectomy in a patient with glycogen storage disease. *Masui* 44(12):1703-1706
7. Reddy SK, Kishnani PS, Sullivan JA, et al (2007) Resection of hepatocellular adenoma in patients with glycogen storage disease type Ia. *Journal of hepatology* 47(5):658-663. doi:10.1016/j.jhep.2007.05.012
8. Saudubray J-M, van den Berghe G, Walter JH (2012) *Inborn Metabolic Diseases. Diagnosis and treatment*, 5th Edition. Springer
9. Däublin G, Schwahn B, Wendel U (2002) Type I glycogen storage disease: Favourable outcome on a strict management regimen avoiding increased lactate production during childhood and adolescence. *European journal of pediatrics* 161 Suppl 1:S40-5.doi: 10.1007/s00431-002-1001-1
10. Bevan JC (1980) Anaesthesia in Von Gierke's disease. *Current approach to management. Anaesthesia* 35(7):699-702
11. Martens, Daniëlle H J, Rake JP, Schwarz M, et al (2008) Pregnancies in glycogen storage disease type Ia. *American journal of obstetrics and gynecology* 198(6):646.e1-7. doi:10.1016/j.ajog.2007.11.050
12. Cohen JL, Vinik A, Faller J, et al (1985) Hyperuricemia in glycogen storage disease type I. Contributions by hypoglycemia and hyperglucagonemia to increased urate production. *The Journal of clinical investigation* 75(1):251–257.doi:10.1172/JCI111681
13. Rake JP, Visser G, Labrune P, et al (2002) Glycogen storage disease type I: Diagnosis, management, clinical course and outcome. Results of the European Study on Glycogen Storage Disease Type I (ESGSD I). *European journal of pediatrics* 161 Suppl 1:S20-34. doi:10.1007/s00431-002-0999-4
14. Melis D, Pivonello R, Parenti G, et al (2007) Increased prevalence of thyroid autoimmunity and hypothyroidism in patients with glycogen storage disease type I. *The Journal of pediatrics* 150(3): 300-5, 305.e1.doi:10.1016/j.jpeds.2006.11.056
15. Bolz D, Stocker F, Zimmermann A (1996) Pulmonary vascular disease in a child with atrial septal defect of the secundum type and type I glycogen storage disease. *Pediatric cardiology* 17(4):265-267
16. Ohura T, Inoue CN, Abukawa D, et al (1995) Progressive pulmonary hypertension: A fatal complication of type I glycogen storage disease. *Journal of inherited metabolic disease* 18(3):361-362
17. Kishnani PS, Austin SL, Abdenur JE, et al (2014) Diagnosis and management of glycogen storage disease type I: a practice guideline of the American College of Medical Genetics and Genomics. *Genetics in medicine: official journal of the American College of Medical Genetics* 16(11): e1.doi:10.1038/gim.2014.128
18. Ubels FL, Rake JP, Slaets, Joris P J, et al (2002) Is glycogen storage disease 1a associated with atherosclerosis? *European journal of pediatrics* 161 Suppl 1: S62-4.doi: 10.1007/s00431-002-1006-9
19. Talente GM, Coleman RA, Alter C, et al (1994) Glycogen storage disease in adults. *Annals of internal medicine* 120(3):218–226

20. Rake JP, Visser G, Labrune P, et al (2002) Guidelines for management of glycogen storage disease type I - European Study on Glycogen Storage Disease Type I (ESGSD I). *European journal of pediatrics* 161 Suppl 1: S112-9. doi: 10.1007/s00431-002-1016-7
21. Wolfsdorf JI, Crigler JF (1999) Effect of continuous glucose therapy begun in infancy on the long-term clinical course of patients with type I glycogen storage disease. *Journal of pediatric gastroenterology and nutrition* 29(2):136-143
22. Weinstein DA, Wolfsdorf JI (2002) Effect of continuous glucose therapy with uncooked cornstarch on the long-term clinical course of type 1a glycogen storage disease. *European journal of pediatrics* 161 Suppl 1:S35-9. doi:10.1007/s00431-002-1000-2
23. Rosenberg H, Davis M, James D, et al (2007) Malignant hyperthermia. *Orphanet J Rare Dis* 2(1):21. doi:10.1186/1750-1172-2-21
24. Carvalho, Patrícia Margarida Serra, Silva, Nuno José Marques Mendes, Dias, Patrícia Glória Dinis, et al (2013) Glycogen Storage Disease type 1a – a secondary cause for hyperlipidemia: report of five cases. *J Diabetes Metab Disord* 12(1):25 doi: 10.1186/2251-6581-12-25
25. Shenkman Z, Golub Y, Meretyk S, et al (1996) Anaesthetic management of a patient with glycogen storage disease type 1b. *Canadian journal of anaesthesia = Journal canadien d'anesthésie* 43(5 Pt 1):467-470. doi:10.1007/BF03018108
26. Yu X, Huang Y, Du J (2009) Bispectral index may not reflect the depth of anaesthesia in a patient with glycogen storage disease type I. *Br J Anaesth* 103(4):616. doi: 10.1093/bja/aep250
27. Takeuchi M, Nohmi T, Ichikawa M, et al (2010) Anesthetic management of a child with moyamoya disease combined with von Gierke's disease. *Masui* 59(2): 260-263
28. Mairovitz V, Labrune P, Fernandez H, et al (2002) Contraception and pregnancy in women affected by glycogen storage diseases. *European journal of pediatrics* 161 Suppl 1: S97-101. doi:10.1007/s00431-002-1013-x
29. Dagli AI, Lee PJ, Correia CE, et al (2010) Pregnancy in glycogen storage disease type Ib: gestational care and report of first successful deliveries. *Journal of inherited metabolic disease* 33 Suppl 3: S151-7. doi:10.1007/s10545-010-9054-1

Last date of modification: October 2015

This guideline has been prepared by:

Authors

Christian Erker, Anaesthesiologist, St. Franziskus-Hospital Muenster, Germany
Christian.Erker@SFH-MUENSTER.de

Michael Moellmann, Anaesthesiologist, St. Franziskus-Hospital Muenster, Germany

Peer revision 1

Marta Inés Berrío Valencia, Anaesthesiologist, Hospital Pablo Tobón Uribe,
Medellín, Colombia
martaberrio@gmail.com

Peer revision 2

Ida Vanessa Doederlein Schwartz, Department of Genetics, Universidade Federal do Rio
Grande do Sul (UFRGS), Porto Alegre, RS, Brazil
ischwartz@hcpa.ufrgs.br
