Case Scenario:

Mohamed is 18 months old. He presents by convulsions in emergency room. He has cold clammy sweat all over his hands and face. His blood sugar is 30mg%. He has huge hepatomegaly, no splenomegaly and no jaundice. His prothrombin time is normal. Mom says he follows at Hepatology Clinic, and he was diagnosed as type III glycogen storage disease. He was advised starch but she does not believe that food can be a medication option, She is non compliant and he keeps getting hypoglycemic attacks. She wants anti-epileptic drugs, or liver transplantation. You admit the child.

1- Do you recommend starch in this boy?
2- Do you recommend dexamethazone in this child?
3- Do you recommend blood transfusion in this child?
4- Do you recommend lactose free diet in this boy?
5- Do you recommend liver transplantation in this boy?
6- Do you recommend stem cell transplantation in this boy?
7- Do you recommend oral prednisone in this child?
8- Do you recommend carbamazepine in this boy?
9- Will you recommend vitamin B for this child?

Model Answer

Title:

Treatment Plan of Infants with Glycogen Storage Disease type III Hypoglycemic Convulsions

Introduction:

Glycogen storage disease type III (GSD type III) is caused by a deficiency of glycogen debrancher enzyme activity. It has variable clinical severity affecting primarily the liver, heart, and skeletal muscle due to accumulation of abnormal glycogen. Deficiency of glycogen debrancher enzyme results in partial breakdown and release of glycogen into glucose causing hypoglycemia. Hypoglycemia compromises conscious level, leads to seizures and can be life threatening. Hypoglycemic seizures are not considered epilepsy. Aim of Work: to define a management plan for an 18 months boy with recurrent hypoglycemic attacks due to GSD type III.

Methods:

We searched the Cochrane reviews and randomized control trials and genetic diseases registry comprising references identified from comprehensive electronic database searches and hand searches of relevant journals and national health institute electronic website.

Results:

We came across 360 researches and case reports describing hypoglycemia and or its management in glycogen GSD type III. A carbohydrate balanced diet with frequent meals and nocturnal continuous tube feeding and addition of uncooked corn starch are the mainstays of treatment to prevent hypoglycaemia. Administration of raw-corn-starch can effectively improve the disease outcome. Hypoglycemia is managed by frequent small meals of uncooked starch, and there is no evidence to support use of anti-epileptic medications in GSD type III induced

hypoglycemia. In hypoglycemic convulsions IV fluids containing glucose is the first line of management. If hypoglycemia is not controlled glucagon is added. Dexamethazone is indicated only if hypoglycemia is not controlled by IV glucose and glucagone. There is no evidence to support the use of oral prednisone in GSD type III to control or prevent seizures. Evidence supports that uncooked starch provides good glycemic control in GSD type III, and no evidence to support use of lactose free diet in control or in prevention of hypoglymic seizures. Vitamin B is indicated in GSD other than type III. Evidence is lacking to support or refrain from using vitamin B. Hypoglycemia induced by GSD type III is not an indication for blood transfusion. Evidence supports improvement of GSD type III by puberty. Liver transplantation is not indicated in children with GSD type III unless he develops cirrhosis or hepatocellular carcinoma. Evidence is lacking to support stem cell transplantation in GSD type III.
Conclusion: In this boy I will start IV fluids containing glucose. I will add glucagon if hypoglycemia is not controlled. I will add dexamethazone as a third line of management. I will recommend compliance to raw uncooked starch. I will not recommend blood transfusion, oral anti-epileptics, lactose free diet, liver transplantation, stem cell transplantation or oral prednisone or steroids. I will recommend a balanced diet containing normal daily requirements of vitamin B and other vitamins.

Key words:
glycogen storage disease type III, hypoglycemia, liver transplantation, dexamethazone, blood transfusion, prednisone, starch, debrancher enzyme.

References:
1- Cheng A, Zhang M, Okubo M, Omichi K, Saltiel AR. Distinct mutations in the glycogen debranching enzyme found in glycogen storage disease type III lead to impairment in diverse cellular functions. Hum Mol Genet. 2009;18(11):2045-52.

2- Froissart R, Piraud M, Boudjemline AM, Vianey-Saban C, Petit F, Hubert-Buron A, Eberschweiler PT, Gajdos V, Labrune P. Glucose-6-phosphatase deficiency. Orphanet J Rare is. 2011; 20;6:27.

3- 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. Glycogen storage disease type III diagnosis and management guidelines. Genet Med. 2010;12(7):446-63.

4- Valayannopoulos V, Bajolle F, Arnoux JB, Dubois S, Sannier N, Baussan C, Petit F, Labrune P, Rabier D, Ottolenghi C, Vassault A, Broissand C, Bonnet D, de Lonlay P. Successful treatment of severe cardiomyopathy in glycogen storage disease type III With D,L-3-hydroxybutyrate, ketogenic and high-protein diet. Pediatr Res. 2011;70(6):638-41.

5- Bernier AV, Sentner CP, Correia CE, Theriaque DW, Shuster JJ, Smit GP, Weinstein DA. Hyperlipidemia in glycogen storage disease type III: effect of age and metabolic control. J Inherit Metab Dis. 2008 Dec;31(6):729-32.

6- Mili A, Ben Charfeddine I, Mamaï O, Abdelhak S, Adala L, Amara A, Pagliarani S, Lucchiarri S, Ayadi A, Tebib N, Harbi A, Bouguila J, H'Mida D, Saad A, Limem K, Comi GP, Gribaa M. Molecular and biochemical characterization of Tunisian patients with glycogen storage disease type III. J Hum Genet. 2012;57(3):170-5.

7- Salemi VM, Demarchi LM, Cabeda EV, Wagenführ J, Tanaka AC. Type III glycogen storage disease mimicking hypertrophic cardiomyopathy. Eur Heart J Cardiovasc Imaging. 2012;13(2):197.

8- Kalkan Ucar S, Coker M, Sözmen E, Goksen Simsek D, Darcan S. An association among iron, copper, zinc, and selenium, and antioxidative status in dyslipidemic pediatric patients with glycogen storage disease types IA and III. J Trace Elem Med Biol. 2010;24(1):42-5.

9- Bernier AV, Sentner CP, Correia CE, Theriaque DW, Shuster JJ, Smit GP, Weinstein DA. Hyperlipidemia in glycogen storage disease type III: effect of age and metabolic control. J Inherit Metab Dis. 2008;31(6):729-32.

10- Iyer SG, Chen CL, Wang CC, Wang SH, Concejero AM, Liu YW, Yang CH, Yong CC, Jawan B, Cheng YF, Eng HL. Long-term results of living donor liver transplantation for lycogen storage disorders in children. Liver Transpl. 2007;13(6):848-52.

11- Matern D, Starzl TE, Arnaout W, Barnard J, Bynon JS, Dhawan A, Emond J,Haagsma EB, Hug G, Lachaux A, Smit GP, Chen YT. Liver transplantation for glycogen storage disease types I, III, and IV. Eur J Pediatr. 1999;158 Suppl 2:S43-8.