I. Introduction

MS was admitted to Primary Children’s Hospital (PCH) on September 30 for a liver transplant. MS had a past medical history of Propionic Acidemia (PA), seizures, developmental delay, gastrostomy dependence, and Diabetes Mellitus (DM) as a result of acute episodes of Pancreatitis. MS had experienced frequent episodes of hyperammonemia, a complication of PA, despite compliance to medical and nutrition treatment. Due to the inability to control ammonia levels, it was determined that a liver transplant was appropriate for this patient. The following case study will discuss the medical nutrition therapy of Propionic Acidemia, as well as review the patient’s medical history, nutrition diagnosis, and interventions.

II. Patient Profile and Social History

MS had a weight of 31.01 kilograms (kg) and a height of 139.8 centimeters (cm) upon admission to PCH. This placed MS’s Body Mass Index (BMI) on the 10th percentile on the Center for Disease Control (CDC) growth chart (Appendix A). Although MS’s anthropometrics plotted in a lower percentile, it appeared that the patient had followed a growth curve just below the third percentile in length-for-age and height-for-age since the age of 2 years (Appendix A). MS’s mental capacity was determined to be at the level of a four year old.

Medical History

MS was diagnosed with PA shortly after birth. Throughout MS’s life, several complications of PA occurred. MS experienced neurological damage, likely caused by recurrent metabolic decompensations, which resulted in developmental delay as well as the development of epilepsy. As mentioned previously, MS was determined to have the brain development of a four year old. MS’s epilepsy was well controlled by Keppra prior to liver transplant. Another complication experienced by MS was multiple episodes of acute pancreatitis. These episodes
were attributed to be the cause of the development of insulin dependent Diabetes Mellitus (DM). MS had a gastrostomy placed to aid in growth. Even though MS had a gastrostomy, the patient still experienced stunted growth, a common complication with PA. Upon admission to PCH, MS had a weight-for-age and a height-for-age plotted below the third percentile on the CDC growth chart for female’s ages 2-20 years (Appendix A). Though the growth chart indicated MS was small, it also showed that MS had followed the same curve on the growth chart since two years of age. Although MS was compliant with all medical and nutrition treatment for PA, MS experienced several episodes of hyperammonemia with increasing difficulty to keep ammonia at a safe level. It was determined that MS would greatly benefit from a liver transplant. MS was admitted to PCH on September 30, 2015 to receive a liver transplant.

**Propionic Acidemia**

Propionic Acidemia is a condition where there is a genetic mutation in the enzyme, propionyl-CoA carboxylase, which is the gene responsible for the catabolism of valine, isoleucine, methionine, threonine, odd chain fatty acids, and the side chain of cholesterol. In the normal breakdown of these substances, propionyl-CoA carboxylase binds to propionyl-CoA which converts these substances into substrates that are used in the Citric Acid Cycle and Gluconeogenesis. Because there is a mutation in propionyl-CoA carboxylase, there is a disruption in the Citric Acid Cycle and Gluconeogenesis. (1) There is also a buildup of the offending amino acids, odd chain fatty acids and the side chain of cholesterol as well as a buildup of propionyl-CoA which is toxic to the human body. (2)

PA is a rare metabolic disorder seen in about 1 in every 100,000 births. It is inherited autosomal recessively. (1) Patients with this condition are usually diagnosed a few days after birth. Signs and symptoms include: poor feeding, vomiting, loss of appetite, lethargy, coma,
encephalopathy, seizure, ketoacidosis, hyperammonemia, and hepatomegaly. Occasionally patients will present with symptoms later in life into adulthood. (3)

PA is included on the newborn screen, but is also diagnosed by testing the activity of propionyl-CoA in skin fibroblasts. This same test can also be performed on hepatocytes and leukocytes. (1) Other tests that can be performed to diagnose PA include arterial blood gas to determine the pH of the body. Also tests for elevated ammonia levels and glycine levels may be used. Ammonia levels greater than or equal to 150 micromoles (umol) and glycine levels greater than 350 umol indicate possible PA. Lastly, the urine can be tested for the level of organic acids using a urinary organic acid assay. (4)

Medical treatment usually begins with the treatment of the patient’s metabolically decompensated state; either before the patient is diagnosed or when the patient is experiencing an episode of metabolic decompensation. According to the proposed guidelines of 2014 for treating PA recommended by Baumgartner et al, discontinuing all enteral feeds until the patient is stable is appropriate. This includes the restriction or elimination of all protein sources to prevent the production of harmful organic acids. One of the main goals of treating PA when a patient is experiencing a metabolic decompensation is to prevent muscle catabolism and promote anabolism. This requires providing the patient with a high amount of calories. This is often accomplished by the administration of a glucose infusion and/or lipid infusion provided via intravenous fluids (IV). (1) An important part of treating a patient experiencing metabolic decompensation is to treat the catabolic stressor that led to the decompensation. These stressors may include viral infections, bacterial infections, injury, and fasting. (1)

Long term treatment of PA includes medical and nutrition treatment that focuses on preventing metabolic decompensations (1). Often patients with PA are prescribed medications
that are meant to reduce the amount of toxic organic acids in the body. One of these medications is a Levocarnitine supplement. This supplement promotes propionylcarnitine synthesis and excretion from the body which results in lower levels of propionic metabolites. (5) Another medication offered is an antibiotic called Metronidazole. This medication targets and kills bacteria in the gut that produces propionic metabolites. By reducing the amount of propionic metabolites in the body, the amount of toxic organic acid in the body is reduced. (6) For long term treatment of PA, the medical team which includes the Registered Dietitian (RD), work together to determine appropriate recommendations and treatment for the patient (1).

If a patient is compliant with medical and nutrition treatment for PA, but continues to experience frequent metabolic decompensations, a liver transplant will be considered as a treatment option. Treatment of PA with liver transplant is something that is being researched. In the past, liver transplants in people with PA have had poor outcomes (7). Recent research shows a more promising outcome where liver transplantation provided patients with PA a better quality of life, fewer metabolic decompensations and less incidence of complications related to PA (7, 8). The liver is responsible for the transamination of valine, isoleucine, methionine, and threonine. For this reason a liver transplant may be an effective treatment option for PA. However, skin fibroblasts and leukocytes also participate in the transamination of these amino acids indicating that a liver transplant may not be enough to completely cure a patient of PA. (7, 19)

One of the main goals of nutrition therapy for PA is to provide adequate nutrition to help the patient achieve optimal growth and development. In general, nutrition therapy for PA includes: providing diet recommendations that provide moderate protein amounts, high calories, and an appropriate metabolic formula. (1) The first step in formulating a diet plan for patients
with PA is to determine their estimated energy needs. These numbers can be calculated using recommendations determined by Acosta and Yannicelli and adjusted per patient case. (9) The following table shows energy and protein intake recommendations for PA as recommended by Acosta and Yannicelli (9).

![Table showing energy and protein intake recommendations for PA](image)

Although protein is limited, consumption of natural protein from food sources is still recommended. However, the amount of natural protein consumed depends on the patients’ tolerance and should be monitored closely. If the patient is unable to tolerate meeting total daily protein needs from protein food sources, then a protein supplement should be considered. Energy requirements should be based on weight gain, or weight loss, and the prevention of catabolism. (1)

In some patients nutrition support is required to prevent catabolism and promote anabolism. The use of nutrition support can prevent overnight fasting that could result in catabolism of muscle. It can also help to provide adequate nutrition when the patient may be experiencing anorexia or feeding difficulties. If nutrition support is needed for long term use, then a gastrostomy is recommended. (1)

There are several different formulas that can be used to help patients with PA to consume adequate nutrients (1). There are four common formulas used: Prophree, Propimex-1, Propimex-
2, and SolCarb (7, 10, 11). Prophree and SolCarb are protein free formulas that provide calories and other vitamins and minerals (10, 11). These formulas may be used when a patient needs more calories, but does not need more protein (10, 11). Propimex-1 contains 15 grams of protein per 100 grams of powder and 480 calories per 100 grams of powder. (10) This formula may be used when a patient cannot obtain the recommended protein intake with natural protein, but also requires more calories. Propimex-2 contains 30 grams of protein per 100 grams of powder and 410 calories per 100 grams of powder. (10) This powder contains a higher amount of protein and fewer calories. This formula may be appropriate for patients who require higher amounts of protein from supplementation. The protein in Propimex-1 and Promimex-2 is in Levo-amino acid form, meaning it is in a broken down state that the body can absorb easily. (10)

Part of the nutrition therapy for PA includes providing the patient with a diet plan to use when they are experiencing a metabolic crisis. This plan should provide a protein recommendation that is lower than normal intake and may recommend elimination of all natural protein from the diet. This plan should give an increased fluid recommendation to aid in the excretion of the toxic organic acids that play a part in the metabolic crisis. Another important aspect of this diet plan is to provide increased calories to prevent muscle catabolism. In some cases the patient will be unable to consume food orally due to severe illness. In this case full nutrition support may be required. As soon as the patient has achieved a more stable state, and clinical conditions improve, the initiation of enteral feeds should commence with an emphasis on the consumption of natural protein. Total parenteral nutrition (TPN) should be initiated if the patient is unable to begin enteral feeds for 24-48 hours. Amino acids should be introduced gradually and supplementation of vitamins and minerals is recommended to prevent nutrient
deficiencies. Nutrition treatment for patients with PA should be individualized and adjusted based on the patient’s tolerance of nutrition therapy. (1, 4)

PA has many complications associated with it. Pancreatitis is a complication for which the cause is not completely understood. One article discussed two possible causes of pancreatitis in PA patients. The first theory is that it is caused at a cellular level because of the mutated enzyme propionyl-CoA carboxylase, which is located in the mitochondria. The theory is that the mitochondria may play a role in regulating adenosine triphosphate and cytosolic calcium levels within the pancreatic acinar cells. When the mitochondrion is dysfunctional, as it is in PA, it may cause elevated levels of calcium in the acinar cells which can cause pancreatitis. (12) Another theory that relates pancreatitis to PA considers the inability for patients with PA to break down odd chain fatty acids. There is evidence to support the theory that hypertriglyceridemia increases the risk of developing pancreatitis. (12) It is thought that because PA patients can have an imbalance of odd chain fatty acids they are at higher risk for developing pancreatitis. (12) Every episode of pancreatitis causes damage to pancreatic cells. Eventually this can lead to the development of insulin deficiency resulting in the development of DM. (13)

Maintaining metabolic balance in patients with PA is a continuous challenge that requires constant medical monitoring. Metabolic decompensations have a number of triggers. These triggers may include noncompliance to medical and nutrition therapy, or the presence of catabolic stressors. Catabolic stressors include fever, viral infection, and injury. Every time a patient experiences metabolic decompensation it can cause neurological damage which can result in a seizure disorder and or developmental delay. (1, 7)

Another complication that can occur with PA is hyperammonemia. This is thought to occur because the organic acids interfere with the urea cycle, which is responsible for excreting
ammonia from the body. In a healthy cell the enzyme succinyl-CoA binds to N-acetylglutamate and is used to initiate the urea cycle. In PA, propionyl-CoA competes with succinyl-CoA in binding to N-acetylglutamate which interferes the urea cycle. This results in a toxic buildup of ammonia in the body. (14, 15)

Cardiomyopathy is a complication of PA for which the cause is very complex and not completely understood. One study examined a patient case of fatal hypertrophic cardiomyopathy in the absence of a metabolic decompensation related to PA. An autopsy revealed low levels of carnitine in the cardiac muscle although there were normal levels of carnitine in the blood and skeletal muscle. The mechanism that caused a deficiency in carnitine in the cardiac muscle is unknown. (16)

Another common complication of PA is restricted growth (7). This occurs because the patient is unable to break down certain amino acids that are essential for growth and development. It can also occur because the patient’s protein intake can be limited to below the amount required to achieve full growth potential. (1, 7)

Management of PA requires constant medical monitoring. Strict medical and diet adherence is key in managing PA and avoiding metabolic decompensations. The medical team must collaborate together and make adjustments in treatment per patient case. (1)

III. Treatment and Progress

MS was admitted on September 30, 2015 for a liver transplant. MS had surgery on October 1, 2015 to receive the deceased donor liver. Following surgery MS was closely monitored for complications. As ordered by the medical doctor (MD), MS was placed on intralipids 20% at 12 milliliters per hour (mL/hr) to provide 576 kilocalories (kcal) as well as Nutren Junior at 10 mL/hr with a goal rate of 40 mL/hr for 24 hours. MS’s intake and diet
recommendations were carefully monitored and adjusted as needed throughout the hospital admission.

**Anthropometrics**

MS’s weight at admission was 31.01 kg with a BMI at the tenth percentile on the CDC growth chart. MS was healthy prior to surgery considering the condition and was following a growth curve directly below the third percentile for both height-for-age and weight-for-age. (Appendix A)

**Biochemical**

Laboratory values prior to surgery reflected an elevated ammonia level, as well as elevated alanine transaminase (ALT), and aspartate aminotransferase (AST) values, which indicated poor liver function. Laboratory values also indicated depressed creatinine which indicated possible reduced muscle mass which was likely related to PA. One day after surgery on October 2, biochemical data showed a continuously elevated ammonia level with increased ALT and AST values which were consistent with the recent liver transplant. Ammonia levels appeared to be trending down post operation. All other nutrition related labs were within normal limits.

(17) * Values in blue indicate low levels. **Values in red indicate elevated levels.

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**Medications**

Notable medications included Levocarnitine; used to supplement carnitine for patients with PA, and to help reduce the buildup of propionic metabolites. MS was also receiving insulin to manage blood glucose levels. Omeprazole was another prescribed medication used to prevent gastroesophageal reflux and ulcers, which may decrease iron and vitamin B12 absorption. MS was also placed on several immunosuppressant and antirejection medications which included; Orapred, Tacrolimus, and Mycophenolate Mofetil. These medications have nutrition side effects that include decreased iron absorption and possible anorexia. It is recommended to have a diet with increased calcium, vitamin D and protein with reduced sodium. (18)

**Clinical Evaluation**

MS had a medical history significant for PA and pancreatitis which eventually lead to the development of diabetes mellitus. MS also had a seizure disorder, which was controlled by medication, and developmental delay at the level of a four year old. MS was dependent on a gastric tube. Because MS experienced several episodes of hyperammonemia, which were difficult to control despite compliance with medical and nutrition therapy, MS was a candidate for a liver transplant. There were no signs of nutrient deficiencies upon assessment.

**Diet Evaluation**

As previously mentioned, MS was dependent on a gastrostomy. Prior to admission it appeared that MS was receiving adequate and appropriate nutrition. Information regarding MS’s home feeding regimen and actual intake were unavailable at the time of assessment. Upon nutrition assessment, MS was receiving intralipids 20% at 12 mL/hr to provide 576 kcals as well as Nutren Jr. at 10 mL/hr with a goal rate of 40 mL/hr. At goal rate MS would receive 960 kcals and 29 grams of protein from Nutren Jr. The total feeding regimen provided 1536 kcals with 29
grams of protein. This regimen was appropriate for post-surgical recovery. However, as MS’s condition improved post-surgery, energy requirements were expected to increase and diet advancement would be appropriate. The RD, genetic team, and medical team worked together to compose an appropriate diet regimen for MS. MS’s estimated needs were calculated based on Acosta and Yannicelli (2001) to be 2300 kcals/day with 60 grams of protein and 1720 mL of fluid per day.

**Diagnosis**

- Impaired nutrient utilization (NC 2.1) related to metabolic disorders as evidence by propionic academia.

Because MS had a diagnosis of PA, the individual was unable to properly break down certain amino acids, fatty acids, and cholesterol (1).

- Increased nutrient needs (NI 5.1) related to wound healing as evidence by liver transplant.

Because of the recent invasive surgery, MS was under metabolic stress and required increased nutrients to meet the requirements for wound healing (4).

**Intervention**

Enteral and Parenteral Nutrition (ND 2)

- A diet regimen was recommended to better meet MS’s estimated needs during recovery from surgery. This regimen was as follows:

Step 1: Continue intralipids 20% at 12 mL/hr.

Step 2: Nutren Jr. with a goal rate of 40 mL/hr. Once goal rate is achieved move on to step 3.

Step 3: Propimex-2 plus Solcarb at 72 mL/hr.
This diet regimen provided 2536 kcals and 79 grams of protein. These recommendations were to aid in recovery from surgery and prevent muscle catabolism. (1, 4) MS’s nutrition goals were:

- Receive adequate intake to promote optimal growth and development for age/condition and to preserve lean body mass.
- Achieve intake of Nutren Jr w/Fiber @ 40 mL/hr + Propimex-2 30 kcal/oz + Solcarb @ 72 mL/hr.
- Advance to oral feedings when clinically indicated.

**Monitoring and Evaluation**

Eight days after surgery, MS’s labs showed an elevated ALT and AST, as well as a high BUN, normal creatinine with abnormal electrolytes (18). The abnormalities in lab values were attributed to MS’s body recovering from surgery (4, 17). Ammonia levels were within normal limits (18).

By day 8 after surgery MS was taking 20% of energy needs by mouth as well as approximately 14% of protein needs by mouth. The RD, genetic team, and medical team reevaluated and adjusted MS’s estimated energy needs to be: 1700-2000 kcals/day, 60-75 grams of protein/day, and 1730 mL of fluid/day. The diet was adjusted to meet MS’s needs as follows:

- Intralipids 20% was discontinued.
- Nutren Jr. continued with an adjusted rate of 30 mL/hr to provide 725 kcals and 21.75 grams of protein.
- Propimex-2 (130 grams): provides 533 kcal, 39 grams protein with Solcarb (118 grams): provides 442.5 kcal, 0 grams protein.
This regimen provided a total of 1700 kcals, 60.75 grams of protein, and 1700 mL of fluid which was appropriate to meet MS’s estimated energy needs. However, it was determined by the genetic team that MS was to receive 1632 kcals, 58.3 grams of protein, and 1632 mL of fluid per day. This was determined with the expectation that MS’s oral intake would continue to improve.

IV. Summary and Conclusion

MS recovered from surgery well and had a good prognosis. Although there is no cure for PA, MS’s symptoms were expected to improve greatly with the possibility of having a more liberalized diet. With a new liver, MS’s body may be able to breakdown the offending amino acids, odd chain fatty acids, and cholesterol side chains. (1, 7, 8) This patient would require close monitoring of diet intake as MS’s diet would need to be adjusted in the weeks following transplant. MS would require monitoring throughout life to continue management of PA, DM, and any other complications that may arise.
V. Nutrition Notes

A. MS dx with propionic academia admitted to PCH for liver transplant. Now day 1 POD. Wt upon admit was 31.01 kg with a BMI at the tenth percentile, height-for-age and weight-for-age below the 3rd %tile. Although MS plots low on growth charts, growth curve has been consistent. Labs were consistent with disease/condition with elevated ALT, AST, and ammonia. Notable meds: Levocarnitine (supplement for carnitine and aids in excretion of propionic metabolites), insulin to manage BG, omeprazole (prevent GERD, decreases iron and vitamin B12 absorption), orapred, tacrolimus, and mycophenolate mofetil (immunosuppressant, antirejection, decreased iron absorption, increase intake of calcium, vitamin D and protein reduced sodium). There were no signs of nutrient deficiencies. MS was g-tube dependent with home feeds of Nutren Jr. Unable to get further information on specific dietary intake. Estimated energy needs: 2300 kcals/day, 60 grams pro, 1720 mL of fluid/day. Total energy intake (FH 1.1.1.1)

D. Impaired nutrient utilization (NC 2.1) related to metabolic disorders as evidence by propionic academia. Increased nutrient needs (NI 5.1) related to wound healing as evidence by liver transplant.

I. Enteral and parenteral nutrition (2)
Step 1: Continue intralipids 20% at 12 mL/hr.
Step 2: Nutren Jr. with a goal rate of 40 mL/hr. Once goal rate is achieved move on to step 3.
Step 3: Propimex-2 plus Solcarb at 72 mL/hr.
  • This diet regimen provided 2536 kcals and 79 grams of protein.
Goals
  • Receive adequate intake to promote optimal growth and development for age/condition and to preserve lean body mass.
  • Achieve intake of Nutren Jr w/Fiber @ 40 mL/hr + Propimex-2 30 kcal/oz + Solcarb @ 72 mL/hr.
  • Advance to oral feedings when clinically indicated.

M/E. RD to f/u in 3 days to assess total energy intake (FH 1.1.1.1) by assessing PO intake.
Follow-up ADIME:

A. No new wt available. Labs indicate improved liver function with normalizing ALT, AST, and ammonia. Noted electrolyte imbalance with elevated BUN and normal creatinine likely caused by stress r/t transplant. Will continue to monitor. Pt achieved PO intake of 20% energy needs and 14% protein needs. Will adjust feeding regimen accordingly.

D. Impaired nutrient utilization (NC 2.1) related to metabolic disorders as evidence by propionic academia.

Increased nutrient needs (NI 5.1) related to wound healing as evidence by liver transplant.

I. Enteral and parenteral nutrition (2)
- Intralipids 20% discontinued.
- Nutren Jr. continued at 30 mL/hr to provide 725 kcals and 21.75 grams of protein.
- Propimex-2 (130 grams): provides 533 kcal, 39 grams protein.
- Solcarb (118 grams): provides 442.5 kcal, 0 grams protein.

This regimen provides 1700 kcals, 60.75 grams protein, and 1700 mL of fluid.

Goals:
- Continue to increase PO intake.
- Preserve LBM.
- Achieve adequate nutrition appropriate for age/condition.

M/E. RD to f/u in 3 days to reevaluate … by checking PO and adjusting feeding regimen as needed.
VI. References


15. Coude FX, Sweetman L, Nyhan WL. Inhibition by Propionyl-coenzyme A of N-acetylgutamate Synthetase in Rat Liver Mitochondria. A Possible Explanation for


