The Restoration Act (INGO) is proudly offering virtual seminars on various clinical topics of inborn errors of metabolism, genetics, and neurology in collaboration with the Ministry of Health Kurdistan Regional Government, Directorate General of Health Duhok, Iraqi & Kurdistan Boards for Medical Specialization/Pediatric, University of Duhok College of Pharmacy and Pediatric Department of Medicine, Kurdistan Pediatric Society, Hevi Hospital, and the Iraqi Pediatric Society.

"Specialized Clinical and Dietary Management of Phenylketonurias"

Held 22 May 2024

Watch the recorded Virtual Clinical Seminar

Presented by Metabolic Specialists:

Dr. Joshua Baker, DO, FAAP, FACMG

Anne Kosek, MS, RD, LDN

Dr. Baker and Ms. Kosek's written answers to written questions asked during the live seminar:

Question: The rate of PKU is increased in World Wide?
Answer: I don't think the rate of PKU is increasing, but more the ability to diagnosis and treat PKU and many different disorders.

Question: Is there a way to diagnose PKU antinatally?
Answer: Yes, but only via genetic testing. You would need to test the PAH gene through CVS or Amniocentesis. This is often not done due to cost and being an invasive risk to pregnancy. Biochemically you cannot test because the mother's liver will keep Phe levels normal for the developing fetus.

Question: If the patient is using Kovan tab, should he restrict his diet or he can eat freely?
Answer: It all depends on the individual response. You would need to monitor levels after starting Kovan to monitor response and protein tolerance. Some are able to eat freely, while many others need some restriction. Kuvan only works for about 50% of patients with PKU.
Answer: note: we need to add that the treatment dose is 20 mg/kg daily. My experience is they give 10 mg/kg daily which is not helping lower the PHE levels

Question: When we label patients unresponsive for Kuvan (BH4)? are they criteria for? In terms of the expected effective duration of treatment before being labeled as unresponsive.
Answer: I would treat a good 2-3 months. However, if the Phe levels are the same after that time, the enzyme is not seeing any benefit from Kuvan.

Question: How do we account for the side effects of treatment due to the low protein intake?
Answer: Monitor nutritional status closely, provide protein-rich diet and supplements as needed, adjust medications if they impact protein metabolism, and utilize a multidisciplinary approach to

manage side effects. Need to monitor vitamin levels and impact on bone health over time if risk for low calcium intake. New formulas have many more vitamins than the ones in the past and are better for overall treatment.

Question: In infants with PKU, to which extent we restrict breast milk and to which ratio compared to medical formula to be given in amount necessary for infants?
Answer: It will depend on each patient and while closely monitoring levels over time. For breastfeeding infants with PKU, it is recommended to start with 1-2 ounces PKU formula prior to the breastfeed to limit total breastmilk intake. Then check a PHE level and adjust PKU formula amount to either increase or decrease total breastmilk intake.

Question: How to improve compliance to medical formulas in PKU infants?
Answer: Typically infants do not have problems with compliance if their families are getting the formula since they drink whatever we give them. We do have to worry about older individuals and making sure they drink their formula and not eat too high of protein.

Question: Is PKU increased in Kurdistan region and especially Duhok City? And is there an apparent risk factors to cause it?
Answer: I think it has always been high, but we are better at diagnosing now. Factors that impact it are common variants in that area, large number of carriers, and multiple marriages between relatives.

Question: Any role of genetic treatment?
Answer: Gene therapy is in development worldwide but still very early in research development.

Question: What about maternal PKU?
Answer: Maternal PKU is very important, in which a woman with PKU has high Phe levels during pregnancy. This can cause developmental concerns such as microcephaly, developmental delay, Small growth, Seizures, and heart defects. Important for any woman with PKU to be monitored VERY closely with frequent levels before and during pregnancy to avoid these complications. For maternal PKU, the recommended treatment range for plasma PHE levels is less than 120 umol/L. An important aspect of the diet to look at and monitor during pregnancy especially of plasma PHE levels are elevated, is total calorie intake. If there are not enough calories consumed, the plasma PHE level is elevated. It is also important to make sure the women gain the appropriate amount of weight during pregnancy.

Question: Significance of phenylalanine deficiency?
Answer: Too low of Phe will have problems with normal growth and development. Will cause hair loss and fragile skin, but worsening height with low levels over time.

Question: Beside the biochemical investigation, what's the most sign that we could diagnose it before doing investigation?
Answer: You can either biochemically test for Phe or genetic testing before symptoms.
If you see a patient with delays, seizures, pale skin, or abnormal urine smell – you should definitely consider PKU and test for this. However, the goal is to find as many patients as possible before symptoms to best prevent complications with early treatment.

Question: I would like to ask about the blood test can be used to detect the disease before the birth?
Answer: You can do carrier testing (genetic) in parents or a test like CVS or amniocentesis for genetic testing before birth. Biochemical testing is not helpful before the baby is born.