INNOVATION OVER THE YEARS: THE CHANGING DEVELOPMENT OF PROTEIN SUBSTITUTES FOR PKU

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Written on behalf of BSNA

Phenylketonuria (PKU) is a rare genetic disorder which, if left untreated, leads to an accumulation of phenylalanine (Phe) and other neurotoxic metabolites. PKU is a rare inherited metabolic disorder detected via newborn screening.[1]

It is characterised by a deficiency of the liver enzyme phenylalanine hydroxylase (PAH), necessary for the conversion of the essential amino acid Phe to tyrosine (Tyr). Deficiency of the enzyme PAH leads to an accumulation of Phe and other neurotoxic metabolites in the blood. Tyr deficiency also occurs due to the limited hydroxylation of Phe to Tyr, resulting in Tyr becoming a conditionally essential amino acid. If untreated, high Phe levels accumulate in the blood and brain, resulting in irreversible intellectual disability, microcephaly, motor deficits, autism, seizures, developmental problems, aberrant behaviour and psychiatric symptoms.[1]

MANAGEMENT OF PKU

The management of PKU is via a complex, lifelong combination of dietary Phe restriction and protein substitutes. A low-protein diet in combination with a low- or Phe-free protein substitute maintains metabolic control. Protein substitutes are classified as Foods for Special Medical Purposes (FSMPs), also known as medical foods, and are essential in the dietary management of this inherited metabolic disorder (IMD), providing individuals with up to 80% of their protein requirements.[1,2] See Figure 1 for the PKU Food Pyramid, which provides a guide to dietary intake.

The main features of dietary management for PKU include a lifelong:[3]

- exclusion of high biological value protein foods to reduce overall protein and Phe intake;
- daily allocation of low biological value protein foods, to provide essential Phe requirements in measured quantities as 50mg Phe exchanges or 1 gram of protein;
- use of protein substitutes containing essential and non-essential amino acids (excluding Phe) and sufficient levels of vitamins and minerals to meet age-specific requirements;[1] many protein substitutes also contain the long-chain polyunsaturated fatty acid, docosahexaenoic acid (DHA);[1]
- liberal use of very-low-protein foods[3] (naturally occurring and manufactured) to meet energy requirements.

CHALLENGES WITH DIETARY ADHERENCE

Adherence to dietary management is a commonly reported challenge in PKU and is known to deteriorate with age.[4] Poor adherence to the diet affects metabolic control and, in turn, impacts mood, attention and cognition.[5] Global factors perceived to positively impact adherence in PKU include the product being palatable and its availability in an attractive, convenient presentation, allowing acceptance amongst peer groups.[4]

There have been many improvements to the range and type of products available for the management of

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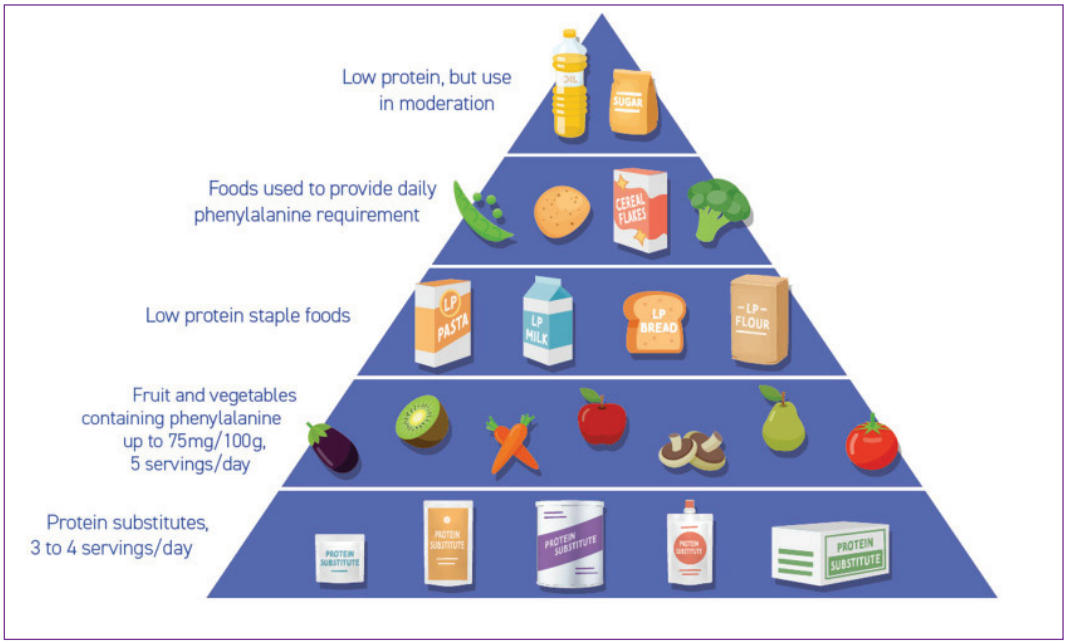
REFERENCES

Please visit: www.NHDmag.co.uk/article-references.html

Figure 1: Food Pyramid for PKU[3]



PKU since the early diets of the 1950s and the introduction of national newborn screening in the UK in 1969. Continued innovation within the medical foods industry, focused on the holistic needs of individuals with PKU, is key in giving choice to individuals with PKU, thereby supporting dietary compliance and improving metabolic control.

Since the 1970s, the dietary management of PKU has relied on the use of synthetic Phe-free amino acid mixtures as the major component of protein substitutes.[6] The taste and smell of these amino acid protein substitutes have been reported as being offensive to individuals with PKU,[7] with commonly reported issues relating to their taste, smell, aftertaste, texture and overall palatability.[8-10]

Given the challenges associated with adherence to protein substitutes, the medical foods industry, along with dietitians working in the field, has searched for innovations that could benefit individuals with PKU in terms of acceptability, tolerance and supporting improvements in dietary adherence. This has been facilitated by advances in technology and manufacturing capabilities, alongside the availability of a wider range of suitable ingredients.[2]

CASEIN GLYCOMACROPEPTIDE (GMP): AN ALTERNATIVE IN THE MANAGEMENT OF PKU

GMP is a whey protein derived from a natural protein source, which, when isolated, naturally contains low levels of Phe, making it suitable for use in the dietary management of PKU.[11] The natural amino acid profile of GMP is not suitable as a sole protein source and supplementation with the limiting amino acids (other than Phe) is therefore required.[1,12]

The first mention of GMP in the dietary management of PKU was published in 2008,[13] with the findings of the first small-scale clinical trial published in 2009.[14] Since then, an ever-increasing interest in the use of GMP in PKU has been documented with both clinical research and an increase in the availability and popularity of GMP-based protein substitutes.

The main differentiating feature and advantage of GMP over amino acids is its superior sensory properties. GMP-based protein substitutes have been widely reported as more palatable in terms of taste and acceptability compared with amino acids[15,16] and generally preferred over amino acid protein substitutes by individuals with PKU.[16,17] Furthermore, it

has been reported that the acceptability of GMP-based protein substitutes supports adherence to dietary management.[18] Fundamentally, the introduction of GMP into the dietary management of PKU has expanded the choice of protein substitutes available to individuals, and dietitians have another offering for individuals struggling with adherence to their dietary regime.

As development continues to progress within the area of GMP-based protein substitutes in line with the latest clinical guidelines and regulatory considerations, patient-centred research is ongoing, with improvements to taste, convenience, choice and volume remaining the key considerations for product innovation.[2] Continued research is also being conducted on the potential additional health benefits of GMP.[19]

BORIS'S STORY

Boris has successfully transitioned to a GMP-based protein substitute; his mother provided insight into the benefits this has provided for both her young child and herself and we provide her feedback here:

"The GMP product has been life-changing. Boris is four years old and has classical PKU. It was really challenging for me and Boris because he didn't like the taste of the previous protein supplement, and I was pregnant and couldn't tolerate the smell. We tried many different substitutes and have continued with the GMP product because my son really likes the taste and I like the smell. He is taking his GMP product three times a day by himself and he is really enjoying it. Boris has been a lot happier than before because it is just so easy to take. His levels are very stable. I have been a lot happier as I don't need to make him take it and I know he is taking the right amount of protein and enjoying it. We have been doing a lot of travelling in the past year and a half. We can just pack his protein substitute and take it with us. It has been so easy for us since we have been on the GMP supplement."

About the British Specialist Nutrition Association (BSNA)

BSNA is the trade association representing manufacturers of products designed to meet the particular nutritional needs of individuals, including specialist products for infants and young children (including infant formula, follow-on formula, young child formula and complementary foods), medical nutrition products for diseases, disorders and medical conditions, including oral nutritional supplements, enteral tube feeding and parenteral nutrition, as well as companies who aseptically compound chemotherapy, parenteral nutrition and CIVAS.