PrescQIPP Community Interest Company

Appropriate prescribing for phenylketonuria (PKU)

Phenylketonuria is the most common inherited protein metabolic disease, with an incidence of approximately 1 in 10,000 births. Restricting dietary intake of phenylalanine (protein) has been shown to be an effective treatment.[1] Nationally over £8.6 million is spent on products specifically for PKU with a further £1.5 million on low-protein foods.[2] Prescribing for these patients can be complex and requires regular review to ensure ongoing appropriateness for the patient's dietary needs.

This bulletin aims to signpost resources that facilitate the appropriate prescribing of low protein foods and protein substitutes for PKU patients. It also provides information on the management of PKU patients including review intervals and the pivotal role of dietitians.

Recommendations

- Ensure that the patient is being prescribed low protein foods for an Advisory Committee on Borderline Substances (ACBS) indication, i.e. inherited metabolic disorders, renal or liver failure requiring a low protein diet.[3]
- Ensure that the patient is assessed by a dietitian before being prescribed a low protein diet. The patient's overall diet and the continued need for a low protein diet should then be reviewed by the dietitian every six months.
- Review quantities of low protein foods being prescribed to ensure appropriateness based on the maximum number of food units per month as well as the age of the patient. Prescribing should neither be excessive nor insufficient for the patient's individual needs. An audit and patient review aid is provided with the bulletin to facilitate this recommendation.
- Ensure prescribing of protein substitutes are in line with recommendations by the patient's dietitian. Review instructions for use and ensure patients take them at least 3 times daily with meals.
- Ensure that quantities and dosages of milk replacements (e.g. Calogen®, Duocal®, Loprofin Drink®, ProZero® and Loprofin Sno-Pro®) and glucose polymer supplements are as recommended by the patient's dietitian.
- Ensure that there is no FP10 prescribing of sapropterin (Kuvan®). This drug is indicated for PKU in pregnancy and is NHS England commissionined in line with their commissioning policy criteria.

Background

Phenylketonuria (PKU) is an inherited metabolic disorder affecting the metabolism of foods containing protein. In people with PKU, the enzyme, phenylalanine hydroxylase, required to convert the amino acid phenylalanine into tyrosine is either absent or deficient. PKU is diagnosed by screening at birth. If untreated, the build-up of phenylalanine in the blood can result in severe brain damage. PKU can be successfully treated by a low phenylalanine diet.[1]

Foods that are naturally low in phenylalanine are not restricted in a low phenylalanine diet. These foods include fruits, some vegetables, fats and oils and sugar. A daily allowance of phenylalanine is permitted made up of 50mg phenylalanine exchanges (equating to approximately 1g protein) from foods such as potatoes, breakfast cereals, and some vegetables. However, as the amount tolerated is only small the daily quantity is usually equivalent to 4-6g of natural protein.[4] The National Society for Phenylketonuria (NSPKU) has produced a detailed booklet on how to calculate exchanges that can be downloaded from their website: http://www.nspku.org/sites/default/files/publications/Exchange%20Info%2007.pdf

The extremely limited number of the naturally low phenylalanine foods available to PKU patients means that they need supplementation with special low protein foods in order to meet daily energy requirements, add bulk to their diet and increase variety. They will also need a protein substitute that contains all essential amino acids except phenylalanine. Many protein substitutes contain vitamins and minerals as well but if not, a separate supplement of vitamins and minerals is needed. In addition to these, milk replacements and glucose polymer supplements are usually necessary and this is determined by the patient's dietitian.[4,5]

Prescribing low protein foods and nutritional supplements in PKU

Low protein special foods

Low protein special foods should ideally provide half of the estimated daily energy requirements in patients with PKU. ACBS indications for prescribing low protein foods include inherited metabolic disorders, renal or liver failure requiring a low protein diet. Thus prescribing low protein foods for individuals with PKU is in line with ACBS criteria.[3,5] Patients with PKU are likely to need a large quantity and variety of products on an ongoing basis. Therefore, rather than specify that patients have a maximum quantity of each food item each month, a maximum number of food units per month for all low protein foods depending on the age of the patient is recommended.[5] The NSPKU has produced a useful list of prescribable low protein foods that can be downloaded from their website: http://www.nspku.org/publications/publication/prescription-items

Protein substitutes

Protein substitutes are available as powders, liquids, tablets, and capsules and can be prescribed for patients with proven PKU in line with ACBS criteria[3,4,5] (See BNF appendix A2.7 for a full list of products). The choice of the protein substitute is always tailored around the specific needs of the patient. The patient's dietitian can provide advice regarding the most suitable protein substitute for the patient. Patients should usually take the protein substitute at least 3 times daily with meals in order to keep phenylalanine levels steady throughout the day, unless their dietitian has advised otherwise.[4]

Vitamins and minerals

Vitamins and minerals must also be included in the diet.[4] If they are not already included in the protein substitute that the patient is taking, their dietitian can advise on the best preparation to take.

Milk replacements and glucose polymer supplements

The need for milk replacements and glucose polymer supplements should be determined on an individual basis by the patient's dietitian.[5]

Review of diet and discontinuation

In the absence of clear evidence there is no consensus as to whether there is a lifelong need for dietary intervention.[1,6,7,8] However, the American College of Medical Genetics and Genomics recently recommended treatment for life in its practice guidelines for PKU.[8] In the UK, the advice of the NSPKU, which is due to be updated this year, is that the continued need for low protein foods should be reviewed

once the patient reaches adulthood. The NSPKU also recommends that patients being treated with a low protein diet should be reviewed every six months and, in view of reports of neurological impairment in a minority of patients, patients not being treated with a low protein diet still require clinical review and should be seen annually. Furthermore, vitamin B12 concentrations should be measured annually in adolescents on a protein restricted diet without amino acid supplements.[1]

Prescribing in pregnancy

Sapropterin (Kuvan®) is a drug licensed for the treatment of hyperphenylalaninaemia (HPA) in adults and children aged over 4 years old with PKU who have been shown to be responsive to such treatment.[9,10] However, sapropterin (Kuvan®) is only commissioned by NHS England for PKU in pregnancy. Therefore, patients being prescribed sapropterin should be reviewed to ensure prescribing is in line with NHS England commissioning policy criteria.[11] There should be no FP10 prescribing of sapropterin (Kuvan®).

Cost to the NHS

The national spend on PKU protein substitutes is £8.6 million and the national spend on low protein foods was nearly £1.5 million (based on the spend between March to May 2014). This does not include the cost of milk replacements and glucose polymer supplements that people with PKU may need as these products are also indicated for other conditions like malnutrition. There was no national spend on FP10 on sapropterin in the last 3 months.

Summary

- Prescribing for PKU patients is complex and requires the involvement of a dietitian to ensure that the patient's diet meets their nutritional needs adequately.
- Regular review is also essential in the management of PKU patients to increase compliance to a low protein diet and reduce long-term complications from the disease.
- The audit tool and review aid provided with this bulletin aims to support these reviews.

Useful resources

The National Society for PKU (NSPKU) website contains detailed information on diet and how to calculate protein exchanges:

- http://www.nspku.org/sites/default/files/publications/Dietary%20Information%20Booklet%202013_0.pdf
- http://www.nspku.org/sites/default/files/publications/Exchange%20Info%2007.pdf

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Additional PrescQIPP resources

 Briefing

 Data pack

 Audit, patient review and data collection form

Available here:

www.prescqipp.info/resources/viewcategory/255-appropriate-prescribing-for-phenylketonuria-pku

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