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Louise and Sarah are Specialist Dietitians working with adults with inherited metabolic disorders, with PKU being their biggest cohort of patients.

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OBESITY IN ADULTS WITH PHENYLKETONURIA

Does following the recommended lifelong restrictive PKU diet bring other nutritional challenges? Problems have been reported in the literature for people with PKU, including non-optimal bone health,¹⁰ nutritional deficiencies¹¹ and obesity.^{12,13}

Newborn screening for the diagnosis of PKU and its treatment with a low phenylalanine (Phe) diet (see Table 1) is one of the major public health success stories of the last century. UK screening began in the 1960s and the heel prick screening test was introduced in 1969. Originally, it was believed that children could cease the low Phe diet once brain growth was complete. However, a growing body of evidence now suggests that people with PKU should remain on a low Phe diet for life.² High Phe concentrations in adults have shown to affect executive functioning and organisational skills,³⁻⁵ lead to trouble with concentration,⁶ cause increased psychiatric symptoms,⁷ slower reaction times⁸ and low mood.^{6,9} It is also believed that there are many older adults in care facilities, where a PKU diagnosis was never originally given.

Our screened cohort of PKU patients at University Hospitals Birmingham is now approaching middle adulthood, with the oldest patients in their 40s. In the UK, we are observing similar levels of obesity in our PKU group as the general population.¹² Other countries have also found similar rates of obesity in children and adults as their general population.¹⁴⁻¹⁷

As our PKU adults age, we question if we will see similar rates of obesity-related co-morbidities as in the general population. Currently, there are no reported cases in the literature of PKU patients with Type 2 diabetes, but in our centre, we had a maternal PKU lady develop gestational diabetes.

The incidence of metabolic syndrome was assessed in a Portuguese PKU cohort, aged between three to 30 years.¹⁴ Although participants had a carbohydrate-rich diet, they did not have a higher incidence of overweight, obesity, central obesity or metabolic syndrome than controls. It was found that triglycerides and HDL were higher and glucose and insulin concentrations were lower than controls.¹⁴ Research into an older group of PKU adults aged between 18 to 57 years found that they had low to normal levels of cholesterol, despite 72% of the group being obese.¹⁸ Results seem to suggest that metabolic syndrome in PKU does not follow the same course as described for the general population and possibly those with PKU have a lower incidence. Further work is needed to look into the mechanisms behind this and potential consequences.

WHAT IS CAUSING THE OBESITY?

There is a lot of speculation as to what could be causing obesity in the PKU cohort. On paper, the PKU diet seems healthy; plenty of vegetables and fruit and avoidance of animal products and, therefore, saturated fat. However, due to the avoidance of natural protein, the PKU diet is higher in carbohydrate and lower in fat and fibre than the recommendations for the general population.^{14,19-21} Are adults on the PKU diet simply not satiated due to the composition of their diet and, therefore, do they consume more calories to make them feel fuller?

PROTEIN

Natural protein promotes satiety and this is obviously restricted in the PKU diet. The protein substitute drinks required (providing all the essential amino acids excluding phenylalanine, vitamins and minerals) are based on amino acids and not whole protein, which could theoretically be less satiating. We are currently hypothesising that, due to this, people are reaching for high carbohydrate, low protein foods to feel full. These could be convenience lower protein snacks which tend to be higher in fat and sugar (crisps, chips, chocolate bars and biscuits), or low-protein prescription foods (low-protein biscuits, cakes and crackers). This may lead to overeating, especially in a non-active PKU patient.

SUGAR AND FIBRE

Recently, new guidelines have been released advising the general population to reduce their sugar consumption to 5% of their energy intake, to prevent excess energy intake and aim to increase fibre intake to 30g a day, thereby decreasing the risk of cardio metabolic disease and colorectal disease.²²

Many of the low-protein foods on prescription, including cereals, biscuits, dessert mixes and cakes, are high in sugar. In the past, these foods have been labelled as 'free' due to low-protein content and, therefore, there is concern that they are freely consumed. Very much like the general population, we are advising that these foods are kept to a minimum in our adults.

Another area of concern is the consumption of sugary, fizzy drinks and fruit juices in the PKU cohort. People with PKU are unable to consume aspartame due to its Phe content. This is a message that is very firmly fixed from childhood and rather than try and find a diet or no-added sugar drink with an alternative sweetener, many adults opt for full-sugar versions. These drinks provide a large quantity of sugar and calories, sabotaging any effort to lose weight. In addition, the promotion of fresh fruit juices and smoothies as a healthy drink has been a message difficult to argue. As most fresh fruit is allowed freely in the PKU diet, we have had to educate the group that consuming the whole fruit is preferable to reduce calorie and sugar intake and also increase fibre consumption.

A high-fibre intake is difficult to achieve following the PKU diet due to the higher protein content of foods containing insoluble fibre (beans, oats, nuts, wholegrain cereals, grains) and low-protein prescription foods being very low in fibre. However, the low-protein foods available on prescription are now realising the niche for fibre and are starting to include more in their products.

EXCHANGE FOODS

The choice of exchange foods could also be an issue. Many of the foods allowed as exchanges (one exchange is the equivalent of 1.0g of protein/50mg of Phe) are high-carbohydrate, for example, chips, crisps, cereal bars and potato products.

Education regarding healthy exchanges and how to incorporate them into a PKU diet is important. For example, normal rice, peas and sweetcorn can be used for exchanges instead of chips, crisps, chocolate and biscuits. For adults with a higher Phe tolerance, we are now encouraging them to include foods containing moderate protein in measured quantities to fit in with allowed exchanges. These include yoghurt, soft cheese, hummus, nuts, normal low-sugar cereals, oats and even eggs for those with a higher protein intake. We believe these foods may be more satiating and reduce the need for regular snacking.

METABOLIC CONTROL

There may be a link between metabolic control and obesity. We found a direct correlation between BMI and Phe concentrations¹² and patients in Portugal were found to have a higher prevalence of overweight and obesity in patients with poor metabolic control.¹⁴

In the USA, they found non-compliant females were more likely to be overweight or obese than compliant females, but no difference in males.²³ High Phe concentrations can affect organisation skills and executive functioning,³⁻⁵ which could affect the ability to plan and cook healthy foods and order low protein foods on prescription.

Patients may find it easier to rely on takeaways and convenience snack foods, but these foods are higher in protein, fat and

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calories. High Phe concentrations also have a negative effect on mood,^{6,7,9} which could negatively affect food choices.

EXERCISE

Exercise and activity in PKU is an area of little research. Anecdotally across the centres, we are getting more reports of people asking for sports nutrition advice for the PKU diet. However, we do not know if activity levels across the PKU cohort are similar to the general population.

It has been speculated that those with higher blood Phe concentrations may struggle with organisation and motivation to exercise which could contribute to overweight and obesity.¹² However, more work is needed in this area.

Table 1: Low phenylalanine diet

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| Avoidance of all foods high in phenylalanine (found in protein), e.g. meat, fish, soya, dairy, pulses, nuts. |
| Protein substitutes (amino acids excluding phenylalanine) taken three to four times per day. This includes ready to drink liquids, powders made into liquids or gels, pudding styles or tablets. |
| Measured amounts of phenylalanine using lower protein foods, e.g. potato, rice, sweetcorn, peas, baked beans - as 50mg Phe (1.0g protein) exchanges if counting strictly or if on a relaxed diet limit to small amounts. |
| Plenty of low-protein foods; naturally occurring or low protein foods on prescription to provide energy and variety in diet (e.g. low protein pasta, rice, bread, flour). |
| Vitamins and minerals are included in the newer protein substitutes, but if not additional vitamins and minerals will need to be taken. |

CONCLUSION

The restricted diet for PKU is not only complex to follow but requires dedication and motivation. Research is showing a number of associated problems, including similar incidence of obesity as the general population. A dietary assessment of a PKU patient should not just be about ensuring low Phe concentrations, but to combine this with a healthy diet to prevent overweight and obesity. We need to spend time to educate patients on the myths and often firmly fixed nutritional beliefs to ensure they are following not only a low Phe diet, but a healthy satiating one as well.

Overtime, we will be able to capture more data on the development of obesity levels and metabolic syndrome and understand further how to help our patients.

Table 2: Tips for a healthy diet for PKU

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| Encourage sugar-free drinks; aspartame-free, sugar-free and diet fizzy drinks and squashes. |
| No more than 150ml a day of fruit juice or smoothie; choose the whole fruit instead. |
| Increase consumption of fruit and vegetables to boost fibre intake. |
| To try a lower sugar protein substitute. |
| Aim to choose high-fibre, low-protein food options on prescription (bread, pasta, crackers). |
| Encourage healthy exchange foods: rice, rice noodles, low sugar high-fibre breakfast cereals, oats, sweetcorn, peas, high-fibre crackers. If higher Phe tolerance: yoghurt, soft cheese, hummus, fromage fraie or nuts. |
| Encourage healthy snacks: fruit, crackers, veg and free dip. Keep snacking on low-protein cakes, biscuits, crisps and desserts to a minimum. |