Restricted eating behavior in children with PKU and HPA

Sarah Bailey

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Committee:

Donna Johnson

Beth Ogata

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Introduction

Restricted eating refers to the practice of limiting the type or amount of food consumed. Many individuals practice restricted eating in an effort to manage food allergies or intolerances, to improve or maintain their health, or as part of an effort to lose or maintain body weight. Parents may restrict the intake of their children for these same reasons. However, Rhee et al found that parental restriction of food in an effort to control weight was actually associated with increased energy intake and unhealthy eating habits in children, including eating in the absence of hunger and disinhibited eating (Rhee et al., 2010). Studies show that these unhealthy habits may be associated with an increased risk of childhood obesity (Thompson, 2010). However, these studies were conducted in a population of typically developing children with parent-imposed restrictions. Little is known about the effect food restriction required for the management or treatment of disease has on children. These therapeutic food restrictions are defined and monitored by medical professionals, but no studies have examined their effect on the eating behaviors of children.

Phenylketonuria (PKU) and hyperphenylalaninemia (HPA) are metabolic disorders that require therapeutic food restrictions. These disorders affect an enzyme required for the conversion of phenylalanine to tyrosine, leading to a build-up of the amino acid phenylalanine (Phe) in the blood. Increased blood levels of Phe are associated with negative neurologic outcomes, including intellectual disability. These negative outcomes are preventable with treatment that includes the restriction of Phe in the diet (Mitchell & Scriver, 1993; Mitchell, Trakadis, & Scriver, 2011).

Phenylketonuria (PKU) and Hyperphenylalaninemia (HPA)

PKU and HPA are both inherited metabolic diseases, a class of genetic disorders usually caused by mutations in enzymes necessary for metabolism. PKU is caused by a deficiency of phenylalanine hydroxylase (PAH); reduced PAH activity decreases the body's ability to break down the amino acid phenylalanine (Phe), leading to increased Phe in the blood. Some individuals have residual PAH function; resulting in a more mild elevation of blood Phe levels called HPA. Because it is possible to prevent negative outcomes with treatment, and because the consequences of non-treatment are severe, PKU is a part of newborn screening programs in all 50 states and many countries around the world. Generally, individuals with plasma Phe greater than 1000 umol/L are diagnosed with classic PKU; HPA is diagnosed in individuals with plasma Phe greater than 120 umol/L but less than 1000 umol/L. However, as newborn screening programs become faster and more efficient babies are being identified and receiving treatment earlier than they had previously, raising controversy over whether it is appropriate to use plasma Phe levels for classification. Currently, some infants with classic PKU may be diagnosed and treated before blood Phe rises above 1000 umol/L, making the cut-off value irrelevant (Blau, van Spronsen, & Levy, 2010; Mitchell & Scriver, 1993). Genetic testing is available to determine the exact type of mutation, or genotype, but reliable information on appropriate and effective treatment based on genotype is not yet available so these tests are not a routine part of diagnosis at many treatment centers (Blau, van Spronsen, & Levy, 2010).

The exact mechanism of the neurological damage caused by untreated PKU is unknown. Phe is a precursor of tyrosine, and dopamine is subsequently synthesized from tyrosine (Tyr). Dopamine is an essential neurotransmitter necessary for signal transmission between nerve cells. Since Phe is not properly metabolized in patients with PKU or HPA, Tyr is limited. That restricts dopamine

synthesis, leading to one possible mechanism for the neurological impairments in individuals with untreated PKU. Alternatively, recent neuroimaging studies have shown white matter abnormalities in the brain of individuals with PKU, even those that were diagnosed early and continuously treated since diagnosis. These abnormalities may reduce the speed with which signals are sent from neuron to neuron, leading to slower information processing. However, receiving treatment was not always associated with good control of Phe levels in these studies. One study found that recent Phe levels were inversely correlated with structural abnormalities found on fMRI images. Therefore, structural abnormalities may be related to elevated Phe and not a separate etiology of neurologic damage (Christ, Moffitt, Peck, White, & Hilgard, 2012; Janos, Grange, Steiner, & White, 2012).

Treatment of PKU and HPA

The goal of treatment of PKU and HPA is to maintain blood Phe concentrations within a range that will prevent the development of neurological complications. For individuals with classic PKU, the ideal range of blood Phe concentrations is 120-360 umol/L (2-6 mg/dL) for early childhood and immediately before and during pregnancy (Mitchell & Scriver, 1993). This range remains ideal over the entire life course, but levels of less than 600 umol/L (10 mg/dL) have been observed in adults without symptoms. Individuals with HPA are often able to maintain blood levels close to the ideal range without treatment, and some experts question whether treatment is necessary for individuals with HPA who consistently have blood Phe concentrations of less than 600 umol/L (10 mg/dL) without treatment (Hanley, 2011; Mitchell & Scriver, 1993).

Dietary restriction is the best studied and most widely used treatment for PKU and HPA. Classic PKU is managed with lifelong dietary restriction of Phe intake. Although some Phe is

necessary for growth and development, the amount of Phe in the diet must be closely controlled to prevent toxic build up in the blood. The amount of dietary Phe an individual is able to consume and remain within the therapeutic range of blood Phe levels is referred to as Phe tolerance. Genotype has not been found to be a reliable predictor of Phe tolerance; so registered dietitians determine Phe tolerance through careful observation and adjustment of Phe intakes (Blau, van Spronsen, & Levy, 2010). Individuals with PKU or HPA require lifelong monitoring of blood levels and Phe intake because Phe tolerance may change with age or changes in BMI and body composition (Rohde et al., 2012).

Since Phe occurs in all high protein foods, it is impossible for patients with PKU to achieve a nutritionally complete diet without the use of high protein, Phe-free formulas. Phe-free formulas provide an adequate amount of protein, as well as sufficient amounts of vitamins and minerals to support normal growth and development (P. B. Acosta et al., 2003). Patients eat a variety of low protein foods in addition to the Phe-free formula in order to consume the limited amount of Phe necessary for development. However, even low protein foods contain some Phe, so individuals must carefully measure portions of low-protein foods to keep their Phe intake below their Phe tolerance level. Because HPA causes a less severe rise in blood Phe levels, Phe-free formulas are not required to maintain blood Phe levels within a safe range. However, the treatment of HPA may include some degree of high protein food restriction in order to maintain serum Phe levels within the therapeutic range. The level of restriction is dependent on the amount of residual enzyme activity.

Although the dietary treatment of PKU is necessary to prevent negative neurological outcomes, the therapeutic diet restricts several nutrients known to be important to normal growth and development. As an essentially vegan diet, natural sources of calcium, omega- 3 fatty acids,

vitamin B12, iron, and zinc are limited. Although Phe-free formulas provide adequate amounts of all of these nutrients, nutrient deficiencies may develop in children who do not drink the full amount of formula prescribed to them (P. B. Acosta et al., 2003). Additionally, PKU may affect the metabolism of other nutrients, possibly resulting in increased needs. Children undergoing dietary treatment of PKU have been observed to have iron deficiency even with iron intakes greater than the RDI. The mechanism for this deficiency is unknown, but supports the need to closely monitor children with PKU for nutritional deficiencies (P. B. Acosta et al., 2004). Some studies had suggested that patients undergoing dietary treatment for PKU developed essential fatty acid deficiencies, and it was hypothesized that this may be because of an inability to form long-chain polyunsaturated fatty acids (PUFAs). However, a 2001 study found no evidence that individuals with PKU synthesized long-chain PUFAs at a decreased rate (P. B. Acosta et al., 2001). As more is learned about the importance of the PUFAs docosahexanoic acid (DHA) and arachidonic acid (AA) for neural development, an increasing number of manufacturers are supplementing PKU formulas with DHA and AA (Agostoni & Heird, 2004; Agostoni et al., 2006).

The dietary treatment of PKU also requires the restriction of dairy foods. Phe- free formulas are supplemented with calcium, but patients who do not drink all of the prescribed formula may be at risk for inadequate calcium intake. Patients who are not fully adherent are also more likely to have elevated blood Phe levels. It is therefore unclear if the lower bone mineral density that is observed in adolescent PKU patients who do not adhere to the diet are caused by inadequate calcium intake or elevated blood Phe levels (Adamczyk et al., 2011). Some evidence shows that reduced bone mineral density (BMD) is present at an early age in individuals with PKU and does not decline further with age. This result is consistent with increased bone turnover

associated with PKU that is not significantly affected by dietary intake of calcium (de Groot, Hoeksma, van Rijn, Slart, & van Spronsen, 2012). However, other studies have found an association between non-adherence to the diet and reduced BMD. Non-adherence to diet may be linked to reduced BMD because individuals who do not follow the dietary restrictions have lower energy and calcium intakes than those who do (Mendes et al., 2012). Interestingly, one study found that all patients being treated for PKU, both those adherent to the diet and those not adherent to the diet, had normal Vitamin D levels (Modan-Moses et al., 2007; Nagasaka et al., 2011).

Additional therapies have been introduced as either a replacement for the therapeutic diet, or as a means to increase Phe tolerance and decrease the level of dietary restriction. These therapies include supplementation with large neutral amino acids (LNAA) and pharmaceuticals that act as a cofactor to residual PAH. LNAA supplementation provided at some treatment centers may allow patients to consume a larger proportion of protein from natural sources, instead of from Phe-free formula (K. K. Ahring, 2010). LNAAs and Phe compete for transporters across the blood-brain barrier. Theoretically, higher concentrations of LNAAs other than Phe in the blood reduce the transport of Phe into the brain thus increasing the blood Phe level that results in neurological damage and therefore Phe tolerance. Recently, a pharmaceutical version of tetrahydrobiopterin (BH4), a cofactor of the PAH enzyme, has become available in the United States. Somewhere between 10% and 60% of patients with PKU or HPA are responsive to BH4 therapy, which reduces blood Phe concentrations and increases dietary Phe tolerance. Responsive individuals are identified through a BH4 challenge. In general, patients with higher Phe tolerance are more likely to respond to BH4 treatment. Genotype has not been a reliable method to predict BH4 responsiveness. Fine-tuning of the appropriate dose and Phe tolerance

over the first year of treatment requires continued close monitoring by both a physician and a dietitian (A. Belanger-Quintana, Burlina, Harding, & Muntau, 2011).

Additional treatments for PKU and HPA continue to be researched. Individual case studies have shown that hepatocyte transplantation allows short term increases in Phe tolerance, but no long-term effects (Stephenne et al., 2012). Another treatment being studied is phenylalanine ammonia lyase (PAL) substitution therapy. PAL catalyzes the deamination reaction of phenylalanine to ammonia and trans-cinnamic acid, which are then excreted in the urine. This allows Phe from the diet to be metabolized into a harmless product that is then eliminated. A clinical trial of subcutaneously injected PAL is currently being conducted based on the findings of previous smaller studies that showed control of blood Phe levels with repeated subcutaneous injections (A. Belanger-Quintana, Burlina, Harding, & Muntau, 2011). This treatment may increase Phe tolerance to the point that diet restriction is no longer necessary.

PKU/HPA and Body Composition

Although the therapeutic diet for the treatment of PKU is necessary to prevent negative neurological outcomes, the restrictive nature of the diet, especially the alteration of the type and amount of protein consumed, raises concerns about growth restriction and alteration of body composition. Protein restriction is known to cause growth restriction in a typically developing population, and while the goal of the therapeutic diet is to provide adequate protein with an appropriate amount of Phe, much of this protein is provided as individual amino acids instead of as complete proteins. Because of concerns that this alteration in protein source might affect growth, studies have examined both the height and body composition of patients with PKU. These studies are limited, at least partially because of the rare nature of the disease; however, a

literature review found that most studies on the subject observed some reduction in height compared to standard growth curves. None, however, observed a reduction in height that was outside a range that was typical for healthy children (Dokoupil et al., 2012). Some of these studies were conducted prior to the year 2000 and therefore do not reflect current practices in the dietary management of PKU (J. R. Allen et al., 1996). Recent studies have found that patients with early detected and continuously treated PKU do not have significant differences in height compared with typically developing peers (M. Huemer, Huemer, Moslinger, Huter, & Stockler-Ipsiroglu, 2007). However, there is some evidence that children with PKU, especially girls, may weigh more than children without PKU (A. Belanger-Quintana & Martinez-Pardo, 2011; Burrage et al., 2012; Scaglioni et al., 2004; J. E. White, Kronmal, & Acosta, 1982). This tendency toward excess weight may be stronger in individuals with the most severe type of PKU (A. Belanger-Quintana & Martinez-Pardo, 2011). One study found a high rate of obesity among children with PKU despite reported energy intakes less than estimated needs, suggesting that PKU may alter metabolic rate. However, this result may have been caused by participants who, either purposely or inadvertently, underestimated their food intakes (P. B. Acosta et al., 2003). Another study found that individuals with PKU had higher body fat percentages across all BMIs. This was especially true of adolescent girls (Albersen et al., 2010). It is unknown if differences in body composition occur primarily because of alterations in metabolism caused by PKU, or as a result of the therapeutic diet. Additionally, the existence of altered body composition in individuals with PKU continues to be debated, with some studies showing no difference in BMI, height, weight, fat free mass or fat mass in children with PKU compared to their typically developing peers (M. Huemer, Huemer, Moslinger, Huter, & Stockler-Ipsiroglu, 2007).

PKU/HPA and Quality of Life

Although normal development is expected in individuals with early and continuously treated PKU, frequent monitoring of Phe levels by blood test and adherence to a restricted diet may affect their quality of life. Phe-free formulas are constructed of individual amino acids instead of plant or animal proteins found in food, and therefore taste different than most conventional foods. This taste may not remain acceptable to individuals with PKU as they try other foods over the course of their life. In general, adherence to diet decreases with increasing age (A. MacDonald, Gokmen-Ozel, van Rijn, & Burgard, 2010). The restrictive diet also sometimes requires individuals with PKU to eat other foods than their friends or family. This can cause some individuals with PKU to feel isolated in social situations. A recent study of Italian children, adolescents and young adults with PKU found that PKU was not experienced by affected individuals as a disease, mainly because individuals with PKU did not feel ill, and did not experience immediate symptoms of PKU if they did not adhere to the diet. However, the participants in this study reported social meal times as a major problem for them due to their fear of stigmatization (Di Ciommo, Forcella, & Cotugno, 2012). Interestingly, this fear does not cause individuals with PKU to report a lower quality of life when compared to individuals without PKU. Studies of Swiss, German, and Dutch children, adolescents, and young adults have all found that individuals with PKU report a similar quality of life when compared to an unaffected age matched group (Bosch et al., 2007; Landolt, Nuoffer, Steinmann, & Superti-Furga, 2002; Simon et al., 2008). The Swiss study found that children with PKU report fewer positive emotions, but have better behavioral adjustment than typically developing controls (Landolt, Nuoffer, Steinmann, & Superti-Furga, 2002). Although individuals with PKU may face problems in social eating situations, PKU or its dietary treatment does not compromise quality of

life or psychological adjustment. However, because issues surrounding quality of life and the experience of illness are culture specific, individuals from other cultures may experience PKU differently. These differences could increase the perceived burden of the disease leading to a decreased quality of life.

Restrictive Eating

Parents create the environment in which children consume food. Parents influence children's eating behaviors through the type and amount of foods they provide, and also through their own eating preferences and behavior at meal times (Birch et al., 2001). Parents may control a child's eating in an effort to change the child's weight status or behavior. One way in which this control may be exerted is through restricting a child's access to foods that are perceived as unhealthy. This practice may be referred to as controlling feeding or restricted eating (Birch et al., 2001; Webber, Cooke, Hill, & Wardle, 2010). Restricted eating has been associated with childhood overweight, and controlling feeding practices have been associated with a decreased ability for a child to respond to their own satiety cues, increasing their risk for becoming overweight (Faith et al., 2004; Francis, Hofer, & Birch, 2001; Thompson, 2010, Johnson & Birch, 1994). Restricted eating has also been associated with unhealthy eating behaviors. Studies have shown that preschool age children ask for and talk more about restricted foods and eat more of the restricted food after the period of restrictions ends. This is true for highly palatable sweet or salty foods as well as for fruit, which is generally perceived as less palatable (Fisher & Birch, 1999b; E. Jansen, Mulkens, Emond, & Jansen, 2008). In both an experimental and a longitudinal study girls with higher levels of restriction reported by either the girl or her mother were more likely to eat in the absence of hunger (Birch, Fisher, & Davison, 2003; Fisher & Birch, 1999a).

Furthermore, girls who reported a parent imposed food restriction were more likely to engage in disinhibited eating, or eating as a result of external cues such as the sight or smell of food, as opposed to internal cues, such as hunger (Carper, Orlet Fisher, & Birch, 2000).

Parents may impose food restrictions because of concerns about weight. Parents who feel their children are more likely to become overweight may impose food restriction in order to decrease this possibility. The cross-sectional studies that have found an association between dietary restriction and overweight cannot show that dietary restriction causes children to be overweight. Instead, they only show that these two occurrences are more likely to occur simultaneously. Children who are overweight may display their genetic potential to be overweight despite an intervention by the parents that includes dietary restriction (Webber, Cooke, Hill, & Wardle, 2010). In fact, a longitudinal study showed that girls who were overweight and had high levels of dietary restriction at age 5 had the greatest increase in eating in the absence of hunger between age 5 and age 9 (Birch, Fisher, & Davison, 2003). Maternal habits also influence the amount of restriction imposed on a child. In an experimental study, a parents' restriction of their own food was associated with maternal restriction of snack foods in girls (Fisher & Birch, 1999a). Although research is unlikely to ever show a causal link between dietary restriction and overweight or obesity, these studies do show that dietary restrictions do not prevent weight issues in children and that they enhance or promote other inappropriate food behaviors.

The treatment for PKU requires dietary restriction in order to prevent neurological complications. It is possible that the alterations in body composition that are observed in some studies of individuals with PKU may be at least partially due to changes in eating behaviors secondary to diet restriction (Poustie & Wildgoose, 2010). There is some evidence that

alterations in eating behavior occur more frequently in children with PKU than in typically developing children. Mothers of children with PKU aged 1-5 years reported a greater prevalence of feeding problems than a group of unaffected, unrelated controls. These feeding problems included poor appetite, a limited range of foods consumed, and difficulty in feeding. Mothers also reported a higher prevalence of gastrointestinal problems in children with PKU (A. MacDonald et al., 1994). This study could demonstrate that children with PKU are at an increased risk of altered eating behavior regardless of dietary restriction. However, the study did not examine parent-feeding practices, so nothing is known about how feeding practices could have influenced the development of child feeding problems.

The Child Feeding Questionnaire

The Child-Feeding Questionnaire (CFQ) is a tool used to assess the self-reported parental beliefs, attitudes, and practices regarding child feeding. The tool also assesses the parents' perception of their child's tendency towards obesity. The tool was developed to quantify the effect of parents' child-feeding practices upon childhood obesity in children 2-11 (Birch et al., 2001). The CFQ measures seven factors using a 5-point Likert scale, with a greater numerical value representing a greater level of concern or restriction. The seven factors measured by the CFQ are perceived responsibility, perceived parent weight, perceived child weight, concern about child weight, restriction, pressure to eat, and monitoring. Four of these factors (perceived responsibility, perceived parent weight, perceived child weight, and concern about child weight) measure perceptions that may influence the use of control in feeding practices, while the other three factors (restriction, pressure to eat, and monitoring) measure parent's attitudes and the use of control in child-feeding (Birch et al., 2001). The CFQ has been validated in racially diverse

groups of American children, as well as in French and Australian children and adolescents (Anderson, Hughes, Fisher, & Nicklas, 2005; Birch et al., 2001; Boles et al., 2010; Corsini, Danthiir, Kettler, & Wilson, 2008; Kaur et al., 2006; A. MacDonald, Rylance, Hall, Asplin, & Booth, 1996; Monnery-Patris et al., 2011).

Purpose

Although the restrictive nature of dietary treatment for PKU and HPA is well known, restricted eating behaviors in children with PKU and HPA have never been assessed. Measuring restricted eating behaviors in children with PKU and HPA would allow the evaluation of the effect that therapeutic restrictions have on behavior changes, and whether these changes are similar to the effects of non-therapeutic restrictions. By administering the CFQ to the parents of children with PKU and HPA, this study will quantify the degree of restricted eating behavior among this population. It was hypothesized that children with more restrictive dietary treatments (PKU) will have higher measures of restricted eating than children with less restrictive dietary treatments (HPA) or their unaffected siblings. Evidence of restricted eating in this population may change the way parents and children are educated about the dietary treatment of PKU and HPA.

Methodology

This study was a cross-sectional design comparing restricted eating behavior, as measured by the CFQ, across three groups: children with PKU, children with HPA, and a control group made up of the unaffected siblings of participants with either PKU or HPA. Participants were recruited from the 249 patients enrolled in the Cristine M. Trahms Program for

Phenylketonuria at the University of Washington (UW PKU Clinic) in Seattle, WA. The University of Washington internal review board approved this study. Eligibility included being between the ages of 2 and 11 years, having a parent that reads English, and having classic PKU or HPA. 178 patients were excluded from the study for being outside of the desired age range. Four patients were excluded because they did not have a parent who could read English, two were excluded for having a different variation of PKU, and one was excluded for having no address listed. Packets were sent to the remaining 64 patients. The packet included an explanatory letter and two copies of the CFQ: one for the child affected by PKU or HPA, and one for an unaffected sibling. Of these 64 patients, 19 were affected by HPA and 45 by PKU. For 7 children with 2 parent addresses listed, the survey was sent to the first parent listed. Three packets sent to the families of children with HPA were returned as undeliverable.

Parents completed the CFQ at home and returned it using a pre-stamped envelope. Parents were also asked to report their child's height and weight, as well as the source of this height and weight. Scores of the CFQ were compared using a t-test with a priori significance set at $p=0.05$.

Results

Thirteen packets were returned, all completed in regard to a child affected by PKU. Five of the thirteen packets included a survey regarding an unaffected sibling. All returned packets were fully completed. No surveys were returned regarding a child with HPA. This represents an overall completion rate of 21% (29% for children with PKU and 0% for children with HPA). The lack of returned surveys regarding children with HPA eliminated the ability of this study to examine the effect of the degree of therapeutic diet restriction on parent feeding practices.

Instead a group of 13 children with classic PKU, all requiring formula and restriction of dietary protein, were compared to 5 siblings not affected by PKU. Children in the group without PKU weighed an average of 9.9 lbs more than children with PKU, and were an average of 16 months older. Neither difference reached statistical significance. There was no difference in BMI Z score between the two groups. Mean heights and weights of the group with PKU and the control group without PKU are shown in Table 1.

Table 1. Mean height and weight			
	Mean +/- standard deviation		
	Children with PKU	Children without PKU	P-value
Weight (pounds)	49.1 +/-14.0	59.0 +/- 29.2	0.50
Height (inches)	44.4 +/- 7.1	46.2 +/- 11.9	0.76
BMI Z Score	0.7 +/- 1.1	0.7 +/- 0.4	1.00
Age (months) at measurement	74.8 +/- 36.0	90.8 +/- 55.7	0.58
Percent Female	42%	40%	

There were no statistically significant differences in mean responses between the group affected by PKU and the group not affected by PKU. These results are presented in Table 2. Although significance was not reached, parents felt more responsibility for child feeding in children affected by PKU, as shown by the perceived responsibility factor of the questionnaire. However, there was also a trend toward less restriction in children affected by PKU. Mean responses for questions measuring the perceived responsibility and restriction factors are shown in Table 3.

Table 2. Mean score responses from the parents' practices, beliefs, and attitudes about child feeding as measured by the Child Feeding Questionnaire

Child Feeding Questionnaire (CFQ) factors	Mean +/- standard deviation		
	Children with PKU	Children without PKU	P-value
Perceived responsibility[1]	4.4 +/- 0.7	4.0 +/- 0.8	0.43
Perceived parent weight[2]	3.1 +/- 0.5	3.2 +/- 0.7	0.82
Perceived child weight[2]	3.1 +/- 0.3	2.9 +/- 0.4	0.41
Concern about child weight[3]	1.5 +/- 0.6	2.1 +/- 1.2	0.30
Restriction[4]	3.2 +/- 0.7	3.6 +/- 1.2	0.49
Pressure to eat[4]	2.5 +/- 1.1	2.3 +/- 1.2	0.72
Monitoring[1]	3.6 +/- 1.2	3.7 +/- 1.2	0.97

[1]Perceived responsibility and monitoring are scored on a 5-point Likert scale: 1=never; 2=seldom; 3=half of the time; 4=most of the time; 5=always.
[2]Perceived parent weight and perceived child weight are scored on a 5-point Likert scale: 1=markedly underweight; 2=underweight; 3=normal;4=overweight;5=markedly overweight.
[3]Concern about child weight is scored on a 5-point Likert scale: 1=unconcerned; 2=a little concerned; 3=concerned; 4=fairly concerned; 5=very concerned.
[4]Restriction and pressure to eat are scored on a 5-point Likert scale: 1=disagree; 2=slightly disagree; 3=neutral; 4=slightly agree; 5=agree.

Table 3. Mean score responses for perceived responsibility and restriction factors of the CFQ			
	Mean +/- standard deviation		
Perceived responsibility	Children with PKU	Children without PKU	P-value
When your child is at home, how often are you responsible for feeding him/her?	4.3 +/- 0.7	4.2 +/- 0.8	0.85
How often are you responsible for deciding what your child's portion sizes are?	4.4 +/- 0.8	3.6 +/- 1.0	0.19
How often are you responsible for deciding if your child has eaten the right kind of foods?	4.4 +/- 0.7	4.2 +/- 0.9	0.72
Restriction			
I have to be sure that my child does not eat too many sweets (candy, ice cream, cake or pastries)	3.9 +/- 1.2	3.8 +/- 1.8	0.95
I have to be sure that my child does not eat too many high-fat foods	3.3 +/- 1.1	3.4 +/- 1.5	0.88
I have to be sure that my child does not eat too much of his/her favorite foods	3.5 +/- 1.2	4.0 +/- 1.0	0.38
I intentionally keep some foods out of my child's reach	3.8 +/- 1.5	3.6 +/- 1.7	0.85
I offer sweets (candy, ice cream, cake, pastries) to my child as a reward for good behavior	2.3 +/- 1.6	3.2 +/- 1.5	0.28
I offer my child her favorite foods in exchange for good behavior	2.3 +/- 1.4	3.0 +/- 1.6	0.40
If I did not guide or regulate my child's eating, she would eat too many junk foods	3.1 +/- 1.4	3.8 +/- 1.6	0.46
If I did not guide or regulate my child's eating, she would eat too much of her favorite foods	3.4 +/- 1.3	4.0 +/- 1.2	0.35

Discussion

It was hypothesized that children with a more restrictive dietary treatment would have higher measures of restricted child feeding. However, this study found that there was no difference between the feeding practices of children with PKU and unaffected siblings without PKU. This result seems to suggest that feeding practices are more affected by parenting style than the presence of a disorder requiring lifelong dietary treatment. It also suggests that

therapeutic diet restrictions do not create the risk for developing unhealthy eating behaviors that non-therapeutic restrictions do. This may be because the current education of families with a child affected by PKU correctly informs parents that children with PKU are expected to develop typically, and although they eat different food than the rest of the family, feeding attitudes and practices should not be different from those for a child without PKU.

This study was not sufficiently powered to detect subtle differences in feeding behaviors between the two groups due to the small sample size. It is possible that the lack of statistically significant results is because the sample is too small to adequately detect a difference and not because a difference does not exist. Since no data has been collected on this subject, these findings serve as a starting point for future studies. A study that would be adequately powered to detect subtle differences in feeding behaviors would require cooperation between several regional clinics and would need to be controlled for differences between the clinics' approaches to education and treatment.

This study was also limited by a response rate of less than 30%. This study was unable to measure the effect different degrees of diet restriction have on eating behavior because all of the respondents had classic PKU, and therefore all required the same degree of dietary restriction. The absence of responses from families of children with HPA may have occurred because families of children with HPA were less likely to feel burdened by the diagnosis, therefore felt less of a connection to the clinic, and were subsequently less motivated to complete the survey. It is possible that a similar self-selection bias occurred in the parents of children with PKU: parents who felt more engaged with the clinic may have been more likely to respond. This may have lead to a greater response rate among those who attend clinic regularly, and therefore are more familiar with the education provided by the clinic. These limitations prevent the findings of this

study from being generalized to all children with PKU, but do provide insight into the effect of education provided at the Cristine M. Trahms Program for Phenylketonuria at the University of Washington on those who regularly attend clinic. Responses to this study were confidential so it is impossible to compare those who responded to those who did not. Possible factors that may have affected whether or not an individual responded include geographic distance from clinic, age of parent, household income, education level, and marital status.

In the small sample represented in this study, children without therapeutic dietary restrictions had slightly higher measures of restrictive child feeding behavior although this difference did not reach statistical significance. There are many reasons a parent might impose restrictive child feeding practices; one of these might be an increased concern about child weight. The results of this study showed a trend toward increased concern about child weight in children without PKU as measured by the concern about child weight factor, although again this difference did not reach statistical significance. Although it is impossible for this study to determine the reason for greater concern about weight in children without PKU, it is interesting to note that both groups had an average BMI z-score of 0.7, demonstrating that concern about child weight differed between the two groups even though relative body fatness, as measured by BMI, did not. It is possible that parents, unaware of research showing a possible trend toward overweight in children with PKU, believe that PKU causes their child to be at low risk for becoming overweight and are therefore less concerned about that possibility.

The mean scores for specific items in the restriction factor show that in this small sample parents are less likely to use food as a reward for good behavior in children with PKU. Using food as a reward is known to be an unhealthy eating behavior that may interfere with a child's ability to recognize hunger and satiety cues and may lead to excess weight (Birch, Zimmerman

and Hind, 1980). In this case, the restrictive nature of the PKU diet may prevent the development of an unhealthy eating behavior.

The trend toward an increase in perceived parent responsibility in children with PKU demonstrated in this sample may reflect the increased burden of weighing and measuring foods for children with PKU during early childhood. Younger children are unable to fully accept the responsibility of determining the amount and type of foods they can and cannot eat. Parents therefore do have more responsibility for determining portion sizes for children with PKU as compared to a child without PKU.

Additional research is necessary to determine if the trends seen in this study apply to a broader population of children with PKU. This includes research to determine if differences in restrictive eating behavior are affected by the degree of therapeutic diet restriction. Further research is also warranted to clarify the impact PKU has on a parent's perception of their child's weight and the impact increased responsibility for determining portion sizes has on the feeding behavior of parents of children with PKU.

Conclusion

In this small sample, parents of children with PKU do not impose a greater degree of dietary restriction on children with PKU compared to unaffected siblings. This result seems to indicate that current education practices at the Cristine M. Trahms Program for Phenylketonuria at the University of Washington correctly inform parents that children with PKU do not require increased diet modifications beyond the therapeutic diet.

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