Home visits in phenylketonuria: a 12-month longitudinal study

Hülya Gökmen-Özel[1], Zehra Büyüktuncer[1], Gülden Köksal[1], H. Serap Kalkanoğlu-Sivri[2], Turgay Coşkun[2]

[1]Department of Nutrition and Dietetics, Faculty of Health Sciences and [2]Pediatric Nutrition and Metabolism Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey

SUMMARY: Gökmen-Özel H, Büyüktuncer Z, Köksal G, Kalkanoğlu-Sivri HS, Coşkun T. Home visits in phenylketonuria: a 12-month longitudinal study. Turk J Pediatr 2011: 53; 149-153.

This study aimed to evaluate the effect of dietary education given to the caregivers of children with phenylketonuria (PKU) in their home environment on children's blood phenylalanine (Phe) levels. Thirty-six children with PKU, aged 2-12 years, were recruited. Each caregiver was visited on three separate occasions and given a detailed dietary education. Fasting morning skin puncture blood samples were collected on Newborn Screening Blood Test filter paper for Phe analysis at baseline and 1, 4, 12, 24, and 48 weeks after the home visits. The mean baseline blood Phe level (365 ± 232 μmol/L) significantly decreased with home visits at the 1st week (314 ± 226 μmol/L) ($p<0.05$). Four weeks after the home visits, the median blood Phe level was still lower than baseline, but the difference was not statistically significant ($p>0.05$). The mean blood Phe levels significantly increased at the end of the 12th, 24th and 48th weeks (329 ± 230 μmol/L; 447 ± 189 μmol/L and 486 ± 261 μmol/L, respectively) ($p<0.05$). A well-controlled blood Phe level can be achieved with intense, regular and continuing education programs, which include regular home visits.

Key words: phenylketonuria, home visits, blood phenylalanine concentrations.

Phenylketonuria (PKU) is an inherited metabolic disease that affects approximately 200 cases per million live births in Turkey. Turkey has a particularly high incidence of PKU compared with other countries, probably due to the relatively recent availability of screening (since 1986) and treatment[1,2].

The goal of PKU therapy is to achieve and maintain normal blood phenylalanine (Phe) levels with minimal episodes of hyperphenylalaninemia, allowing normal physical and mental growth and development. A Phe-restricted diet is the mainstay of PKU treatment, and in recent years, the nutritional management of PKU has become more complex in order to optimize patients' growth, development and dietary compliance[3]. Although the importance of dietary compliance in PKU treatment is well-explained to parents or caregivers as a part of the education program, a high percentage of blood Phe concentrations are still above target ranges[4,5]. Dietary compliance is influenced by cognitive, emotional, physiological, and cultural factors. Patients and caregivers vary in their willingness and capacity to adhere to dietary treatment depending on these factors. Although more education does not always result in improved compliance, intense and continuing education programs are certainly important in helping to optimize dietary compliance[6]. Many teaching initiatives in order to improve compliance have been reported. These include home visiting, teaching booklets, games, teaching schools, culinary workshops, and social events[7].

Home visits are done by registered dietitians and play a vital role in providing optimal nutrition care and contributing to each patient's quality of life. Home visits have several advantages in that they improve nutritional status, provide chronic care management and help patients become more independent. Four

Source of financial assistance: This study was supported by Nutricia Advanced Medical Nutrition (Turkey).

major types of home visits have been described in the literature for dietitians: illness visits, visits to dying patients, home assessment visits, and follow-up visits after hospitalization. The American Dietetic Association strongly recommends that illness home visits by a registered dietitian should include nutrition screening, nutrition assessment, nutrition diagnosis, patient/parent education and counselling, monitoring, and follow-up[8]. Some inherited metabolic disorders (IMD) centers in Europe provide home visiting services for patients with PKU. Although Turkey has one of the highest PKU prevalences[2], none of the health professionals do home visits routinely, and there is no system that evaluates how a diet is applied practically at home. Therefore, this study aimed to evaluate the effect of practical dietary education about PKU given to the patients/caregivers in their home environment on the children's blood Phe concentrations for a 12-month period.

Material and Methods

Forty-eight children with PKU were chosen from two different cities (Ankara and Konya), since the number of PKU patients was higher in these cities compared to the other regions. Patients/caregivers who were not able to take sufficient blood (n=3) or did not send the blood samples (n=9) to the study center were excluded. The remaining 36 patients, 21 girls (58.3%) and 15 boys (41.7%), with a median age of 8 years (range: 2-12 years) were recruited. They were all treated by the Metabolism Unit of Hacettepe University İhsan Doğramacı Children's Hospital. There were three inclusion criteria: subjects were (1) aged 2-12 years; (2) diagnosed by neonatal screening; and (3) followed a strict low-Phe diet. Exclusion criteria included: (1) not following the strict low-Phe diet and (2) patients/caregivers not able to take blood samples at home.

All patients followed a strict low-Phe diet comprising: (1) a dietary Phe allocation using a 15 mg Phe exchange system; (2) a Phe-free protein substitute; and (3) special low-protein foods permitted in usual quantities. The median daily allocated Phe and protein intake were 20 mg/kg (range: 15-60 mg/kg/day) and 1.2 g/kg (range: 1-2 g/kg/day), respectively. The study was approved by the Ethical Committee for Medical, Surgical and Drug Research at Hacettepe University Faculty of Medicine, Ankara, Turkey (09.11.2006, HEK 06/123-23). Informed consent was obtained from all parents.

Study Design

This was a 12-month, single center, longitudinal study. Each mother/caregiver was visited on three separate occasions by a pediatric dietitian. A questionnaire including the social and educational background of parents/caregivers, the management of PKU on a daily basis, characteristics of the diet therapy including protein substitute amount, type, timing, and frequency, and preparation of low-protein foods was administered.

A dietary education program was given at the beginning of the study following the collection of a three-day baseline blood sample. The program aimed to improve the practical and theoretical knowledge of the dietary management of PKU. Practical issues addressed were regular intake of protein substitute (amount, type, timing, frequency) and low-protein food preparation. Practical demonstration was used in addition to the provision of visual materials such as leaflets, photographs, food models, and recipes with low-protein products.

Skin puncture blood specimens were collected on Newborn Screening Blood Test filter paper (Guthrie cards) for Phe analysis by the patients/caregivers for three days during the baseline and at the end of weeks 1, 4, 12, 24, and 48. Blood samples were taken during the study period at the same time each day, before breakfast, under fasting conditions.

Blood Phenylalanine Analysis

Blood samples that had been collected on the Guthrie cards were immediately posted to Hacettepe University İhsan Doğramacı Children's Hospital Metabolism Unit laboratories, where they were analyzed for Phe by tandem mass spectrometry (MS). At the beginning of the study period, instruction regarding the blood collection technique was given and the caregiver's competency was assessed by the dietitian. The blood-sampling equipment, envelopes and stamps were supplied. Blood Phe concentrations were classified according to the Medical Research Council (MRC) Working Party guidelines

(MRC1993)[9] as: subjects 2-5 years old, 120-360 μmol/L and subjects 6-12 years old, 120-480 μmol/L.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) for Windows version 11.5 was used for statistical analysis. The normality distribution of the data was checked using the Kolmogorov–Smirnov test. The results were given as mean, standard deviation, median, minimum, and maximum values. Since the distribution was not normal, nonparametric tests were used. Mann–Whitney test was used to compare the blood Phe levels of patients according to their background characteristics, and Friedman and Kruskal–Wallis tests were performed for comparison of blood Phe levels of each child at the different periods of the study. A p value <0.05 (two-tailed) was considered significant.

Results

There was no significant difference in mean baseline blood Phe levels with respect to age groups, gender, maternal/paternal employment, and educational status. Twenty-two (61%) children took their protein substitutes three times a day or more frequently. Protein substitutes were taken as a high-volume liquid. Twenty-six patients (72%) preferred to mix the protein substitutes with sugar, cornstarch or fruit juices. The baseline mean blood Phe concentrations in patients who took the protein substitute less than three times a day were not found statistically different than in those who took the protein substitute three times or more. Six patients (17%) did not consume low-protein special products, due to their high prices, unpalatability and the lack of cooking skills of the mothers/caregivers. The baseline mean blood Phe concentrations in patients who did not consume low-protein special products as a part of their diet were higher than in those who did consume low-protein special products regularly, but the difference was not statistically significant.

The mean blood Phe levels at the 1st week of the study (314 ± 226 μmol/L) decreased significantly compared to the baseline (365 ± 232 μmol/L) (p<0.05, Fig. 1). Although at the end of the 4th week, the mean blood Phe levels (329 ± 230 μmol/L) were still decreased compared to the baseline, the difference was not statistically significant. The mean blood Phe levels at the end of the 12th week (385 ± 238 μmol/L) had returned to the baseline levels. However, a significant increase in the mean blood Phe levels at the 24th and 48th weeks was determined when compared to the baseline (447 ± 189 μmol/L and 486 ± 261 μmol/L, respectively, p<0.05). The mean blood Phe levels measured after the 24th and 48th weeks of the study were also significantly higher than the 1st and 4th week values (p<0.01).

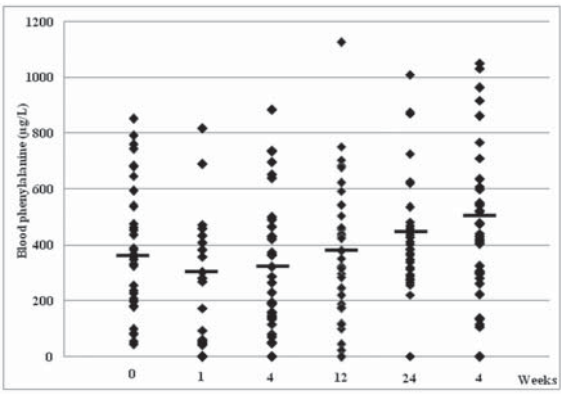

Fig. 1. Changes in blood Phe levels over time.

Twenty-eight percent of the subjects' baseline blood Phe levels were above age-related reference ranges. The blood Phe concentration seemed to be higher in school-age children (mean: 391 ± 240 mmol/L; range: 44-852 mmol/L) than in preschool children (mean: 312 ± 217 mmol/L; range: 46-682 mmol/L), but the difference was not statistically significant (p=0.295). After the 1st week of the home visits, 11% of the patients' blood Phe levels were above the recommended ranges. However, this percentage increased at the 4th, 12th, 24th, and 48th weeks of the study compared to the baseline and the 1st week (31%, 30%, 36%, and 53%, respectively).

Discussion

Since a low-Phe diet is one of the most restrictive of all dietary treatments, adherence to the diet is very difficult[10] and influenced by many factors: parental application and supervision, the level of knowledge of the parents and caregivers, motivation, and parental organizational skills[11,12]. Intense and continuing education can help to ensure that patients and

their families understand the diet, improve the motivation of the patients and their families, and generate a positive attitude towards the diet, eventually resulting in the achievement of blood Phe control[7,13,14].

Although many IMD centers organize dietary education programs to improve parental coping ability, the efficiency of those programs needs to be improved in some countries. In the last decade, the major problem encountered in the management of PKU in Turkey was the late onset of treatment, because the newborn screening program covered about only 40% of the country[2]. Although the program covers all metropolises at present, the control of normal blood Phe concentrations is still an important issue, and many difficulties remain in the achievement of normal blood Phe concentrations, including: a limited number of experienced clinics for treatment, lack of experienced physicians/dietitians, lack of a frequent blood Phe monitoring system due to difficulties in the transport of the blood samples to the laboratories, large families, illiteracy and ignorance of the parents, and lack of published information about Phe and amino-acid content of some foods[11]. In this study, according to baseline values, 28% of the children had blood Phe concentrations above the recommended levels. This was similar to previous reports in other studies[2,4,5,11].

Data regarding the efficiency of home visits on metabolic control of blood Phe are very limited. It is clear that home visits provide an important opportunity to identify specific factors related with home environment that influence dietary adherence, and this is essential to provide an efficient support to the family in the management of the disorder. A home visit service can provide ongoing education for the child with PKU and the family, leading to a greater understanding and better overall metabolic control, and serves as a liaise with other professionals involved with the child and family to ensure continuity of care. In this study, we evaluated the effect of dietary education given to the caregivers of children with PKU in their home environment on children's blood Phe levels. This intervention might be considered as a small pilot study for a home visiting service. Our findings suggest that dietary education directed at providing both theoretical and practical support and encouraging positive attitudes in patients in their home environment is likely to be successful in the short term. However, the efficiency of the program in the long term requires regular ongoing education reinforcement and support. For the organization of a home visiting service including dietary education, the following seem to be the crucial steps: identify a well-defined geographic target area, rally local health professional support and engage community clinic personnel, provide in-services to area hospitals to initiate referrals and gain provider trust, use a professional-based model of care, obtain non-profit status to apply for a variety of funding, and hire staff who are knowledgeable about the cultural needs of the community[15]. On the other hand, the time-consuming nature of home visits, the relatively poor remuneration associated with them, a large part-time workforce, and concerns about personal safety may all contribute to increasing reluctance among health professionals to undertake this type of consultation. In this context, it is essential to ensure that enough health professionals are available and that medical resources are organized efficiently enough to provide adequate home care services[16]. Furthermore, though it is well-known that dietitians play a vital role in providing optimal nutrition care and contributing to each patient's quality of life, the limited use of dietitians in home visits is primarily due to the lack of reimbursement and insufficient number of specialized dietitians.

Although this group of caregivers had received a comprehensive teaching program in the early years, new strategies are required for the small sub-section of families who have the least knowledge of PKU and limited educational qualifications. A variety of approaches rather than any one type of teaching method is more likely to be effective. Any teaching program must consider individual differences in capacity to process information, and it should be supportive and inclusive of extended family members who commonly have an invaluable role to play in diet therapy. More practical training with tasks such as planning appropriate menus, food shopping, measuring ingredients, and cooking low-protein dishes may give caregivers confidence in their own ability to adhere to the treatment regimen[17]. Others

measures may include providing models of positive behavior through working alongside other caregivers or even older patients with PKU[18].

The present study has several limitations. Only a small numbers of subjects were studied due to difficulties in reaching the patients/families. Caregiver motivation and ability to cope were not assessed. However, all the data were objective, collected in the same standardized manner, and all the patients had been taught by the same dietitian in the same systemized way.

We hope to see the establishment nationwide of a home visit program for people with PKU to understand better which factors at home affect blood Phe concentrations. This will provide a PKU service that will meet the needs of the children, their parents and perhaps the National Framework.

Acknowledgement

The authors thank chemical engineer Saniye Onol and biologist Yelda Dogan for their contribution to analyzing the blood Phe levels; Pınar Kasapoğulları and Nesli Arpacı, Nutrition and Dietetics students at Hacettepe University, for their contribution to collecting data; and all patients and parents who participated in this study. This study was supported by Nutricia Advanced Medical Nutrition (Turkey).

REFERENCES

1. Tuncbilek E. Clinical outcomes of consanguineous marriages in Turkey. Turk J Pediatr 2001; 43: 277-279.
2. Ozalp I, Coskun T, Tokatli A, et al. Newborn PKU screening in Turkey: at present and organization for future. Turk J Pediatr 2001; 43: 97–101.
3. Feilet F, Agostoni C. Nutritional issues in treating phenylketonuria. J Inherit Metab Dis 2010; 33: 659-664.
4. Walter JH, White FJ, Hall SK, et al. How practical are recommendations for dietary control in phenylketonuria? Lancet 2002; 360: 55-57.
5. Ahring K, Belanger-Quintana A, Dokoupil K, et al. Dietary management practices in phenylketonuria across European centres. Clin Nutr 2009; 28: 231-236.
6. MacDonald A, Gokmen-Ozel H, van Rijn M, et al. The reality of dietary compliance in the management of phenylketonuria. J Inherit Metab Dis 2010; 33: 665–670.
7. MacDonald A. Diet and compliance in phenylketonuria. Eur J Pediatr 2000; 159 (Suppl): 136–141.
8. Practice Paper of the American Dietetic Association. Home care-opportunities for food and nutritional professionals. J Am Diet Assoc 2009; 109: 1092-1100.
9. Medical Research Council (MRC) Working Party on Phenylketonuria. Recommendations on the dietary management of phenylketonuria. Arch Dis Child 1993; 68: 426–427.
10. MacDonald A, Rylance GW, Asplin DA, et al. Feeding problems in young children with PKU. Acta Paediatr Suppl 1994; 407: 73–74.
11. Gokmen Ozel H, Kucukkasap T, Koksal G, et al. Does maternal knowledge impact blood phenylalanine concentration in Turkish children with phenylketonuria? J Inherit Metab Dis 2008; June 27 (Epub ahead of print).
12. MacDonald A, Daly A, Davies P, et al. PKU At Home: An Observational Study. Dietary Management of Inborn Errors of Metabolic Disease, Royal College of Physicians. London: Inborn Error Review Series; 2004: 14: 8.
13. Levy HL, Waisbren SE. PKU in adolescents: rationale and psychosocial factors in diet continuation. Acta Paediatr Suppl 1994; 407: 92-97.
14. National Institutes of Health Consensus Development Panel. National Institutes of Health Consensus Development Conference Statement: phenylketonuria: screening and management, October 16–18, 2000. Pediatrics 2001; 108: 972–982.
15. Hedges S, Simmes D, Martinez A, et al. A home visitation program welcomes home first-time moms and their infants. Home Healthcare Nurse 2005; 23: 286-289.
16. Joyce C, Piterman L. Trends in GP home visits. Aust Fam Physician 2008; 37: 1039-1042.
17. Waisbren SE, Rokni H, Rohr F, et al. Social factors and the meaning of food in adherence to medical diets: results of a maternal phenylketonuria summer camp. J Inherit Metab Dis 1997; 20: 21-27.
18. Sherman AM, Bowen DJ, Vitolins M, et al. Dietary adherence: characteristics and interventions. Controlled Clinical Trials 2000; 21: 206-211.