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The Effects of Breastfeeding in Infants With Phenylketonuria

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ABSTRACT

Purpose: In the early years of phenylketonuria (PKU) treatment, mothers and healthcare professionals often decide to discontinue breastfeeding after the diagnosis of PKU in infants. It was believed to be the only effective way to monitor the infant's intake and allow for precise titration and measurement of the intake of phenylalanine (Phe). In the early 1980s, with the determination of low concentration of Phe in breast milk, breast milk supplemented with Phe-free formula has become an acceptable dietary treatment for infants with PKU. Today, breastfeeding is encouraged and well established in PKU patients.
The aim of the present study is to investigate the prevalence and duration of breastfeeding, the effect of breastfeeding on serum Phe levels, and weight gain in infants with PKU.
Design and Methods: Data were collected from chart reviews. Medical records of 142 children with PKU diagnosed via the national neonatal screening program were analyzed retrospectively.
Results: Of the 41 infants with complete medical records, 40 (97.6%) were breastfed following delivery whereas only one (2.4%) was bottle fed. After the diagnosis, breastfeeding was continued in 25 (61%) infants with phenylalanine-free amino acid based protein substitute. The mean duration of breastfeeding was 7.4 ± 4.0 (1–15) months. Serum Phe concentration of breastfed infants (280 ± 163 μmol/L) was significantly lower than non-breastfed infants (490 ± 199 μmol/L) ($p < 0.001$). Mean monthly weight gain in the first year of life was significantly higher in breastfed patients (493 ± 159 g/month) compared to non-breastfed patients (399 ± 116 g/month) ($p = 0.046$).
Conclusion: In the first year of life, weight gain and serum Phe levels were more favorable in breastfed infants with PKU compared to non-breastfed infants with PKU.

Background

Phenylketonuria (PKU) is a congenital disorder of the phenylalanine (Phe) metabolism caused by mutations in the liver enzyme, phenylalanine hydroxylase, encoded by the phenylalanine hydroxylase (PAH) gene (OMIM 261600) (Blau, van Spronsen, & Levy, 2010). Phenylalanine hydroxylase deficiency results in the inability to convert Phe to tyrosine, leading to increased phenylalanine concentrations in blood and central nervous system. The dietary treatment of PKU is based on the restriction of Phe intake in order to maintain blood Phe concentrations within the recommended range (MacDonald, Rocha, van Rijn, & Feillet, 2011). Unless the affected child is maintained on a strict low-phenylalanine diet, PKU leads to mental retardation, seizures, behavioral problems, and other neurological symptoms. In contrast, when identified via newborn screening and if treatment is initiated before one month of age, cognitive–neurological development is preserved essentially normal (Vockley et al., 2014). Individuals with PKU must maintain a life-long protein-restricted diet (Feillet & Agostoni, 2010).

Breastfeeding provides an ideal food for healthy growth and development of infants and children. Optimal breastfeeding practice includes timely initiation of breastfeeding, exclusive breastfeeding for the first six months and continued breastfeeding up to the age of two years and beyond along with appropriate complementary feeding (World Health Organization [WHO], 2003). Unfortunately, exclusive breastfeeding for the first six months of life affects the cognitive–neurological development of patients with PKU as the Phe in breast milk cannot be converted to tyrosine by the phenylalanine hydroxylase enzyme in liver. Formerly, the standard of care for infants diagnosed with PKU was immediate discontinuation of breastfeeding to maintain appropriate Phe levels with the combination of standard commercial infant formulas and phenylalanine-free amino acid based protein substitute. In 1980, with the discovery of lower Phe levels in human breast milk compared to standard commercial infant formulas, breastfeeding has begun

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to replace the standard commercial formula in protein-restricted diet of patients with PKU (Ernest, McCabe, Neifert, & O'Flynn, 1980; Motzfeldt, Lilje, & Nylander, 1999). Today, breastfeeding is encouraged and well established in PKU patients (Banta-Wright, Shelton, Lowe, Knafl, & Houck, 2012; Kanufre et al., 2007; van Rijn et al., 2003).

Previous studies showed that breastfed infants with PKU had no significant differences in weight gain, daily Phe intake and mean serum Phe concentrations compared to bottle-fed infants with PKU (Cornejo et al., 2003; Demirkol et al., 2001; Kanufre et al., 2007). On the other hand, recently Banta-Wright et al. (2012) revealed that mean serum Phe level in breastfed infants is lower than bottle-fed infants with PKU.

In this study, our aim was to determine the prevalence and duration of breastfeeding, the effect of breastfeeding on serum Phe levels, and weight gain in infants with PKU. We also aimed to investigate the factors related to duration of breastfeeding in infants with PKU to provide information to better evaluate the effect of breastfeeding in infants with PKU, a subject for which limited results have been reported previously in the literature.

Methods

Design

The data for this study were collected by means of a retrospective chart review. Medical records were analyzed from 2008 to 2016 period for patients with classic PKU (serum Phe level above >1200 μmol/L at diagnose) admitted to Pediatric Nutrition and Metabolism Unit, a baby friendly hospital located in the Aegean Region in western Turkey. Patients with incomplete records or insufficient data were excluded from the study (Fig. 1). This study has been granted approval by the University Research Ethics Board.

Study Population.

The medical charts of 142 children with PKU admitted to our center were analyzed retrospectively. Infants with incomplete medical records (weight data, feeding information and serum Phe level), missing demographic data (parental consanguinity, gross annual household income, maternal education level, parity of the mother, place of residence, first breastfeeding experience of the mother), irregular follow-up (the study included only patients who were examined at least once a month) and low adherence to diet (patients who were not fed according to diet list and/or patients who were fed both breast milk, commercial formula and phenylalanine-free amino acid based protein substitute) were excluded from the study (Fig. 1). Forty-one of the subjects had complete medical records and were enrolled in the study.

Setting

Infants were categorized as breastfed and non-breastfed according to the type of feeding after PKU diagnosis. Infants who were fed with the combination of commercial formula (Aptamil®, Milupa [1.4 g protein and 60 mg Phe in 100 mL]; Bebelac® [1.4 g protein an 58 mg Phe in 100 mL]) and phenylalanine-free amino acid based protein substitute (PKU Anamix Infant®, Nutricia; Comida-PKU A®, ComidaMed) after the diagnosis of PKU were included in the non-breastfed group. Infants who continued to be breastfed together with the phenylalanine-free amino acid based protein substitute after the diagnosis of PKU were included in the breastfed group. In breastfed group, phenylalanine-free amino acid based protein substitute was given after each breastfeeding. In non-breastfed group, combination of commercial formula and phenylalanine-free amino acid based protein substitute was served at each feeding. At least every month, all patients diet lists were adjusted and the volume of phenylalanine-free amino acid based protein substitute and commercial formula were revised. In non-breastfed group, daily protein consumption was determined according to dietary reference intake (DRI). Amount of Phe consumed was adjusted between 40 and 70 mg/kg/day according to serum Phe level.

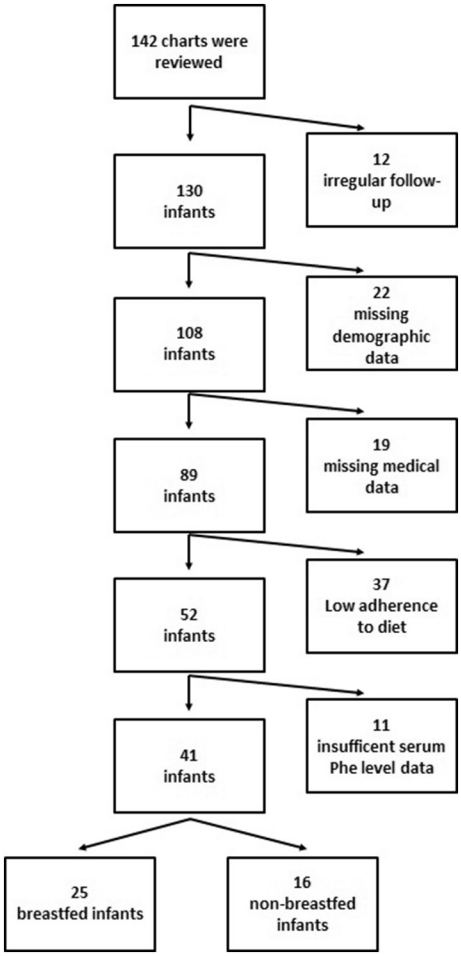

Fig. 1. Consort flow diagram and reasons for exclusion.

Data Collection

Demographic data (according to the information provided by the family and medical records; age at the time of diagnosis, gender, parental consanguinity, gross annual household income, maternal education level) and clinical and laboratory findings (based on physical examination, clinical and dietitian's records of infants who were assessed at least once a month; birth weight, daily weight gain of patients during the breastfeeding period, monthly weight gain in the first year of life, duration of breastfeeding, serum Phe level) of the patients were documented. No clinical application and absence of serum Phe values recorded at least once a month were defined as insufficient medical records and were determined as exclusion criteria. In the analysis of mean Phe levels (data were collected from the electronic document management system of the hospital), newborn-screening and confirmatory diagnostic serum Phe levels which were >1200 μmol/L and skewed the data were excluded for each patient. For the study, all data were collected by physicians working in the pediatric nutrition and metabolism department.

Data Analysis

Statistical data analyses were performed with the SPSS computer software (version 15.0; SPSS, Chicago, IL). While categorical data were expressed as number, percentage (%), continuous data were expressed as mean ± standard deviation (minimum-maximum). Kolmogorov-Smirnov test was performed to examine the normality of parameters. Categorical variables (gender, parental consanguinity, gross annual