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Review Article

Association of Quality of Life with Serum Phenylalanine Level and Socioeconomic Status in Patients with Phenylketonuria: A Review

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ABSTRACT

Phenylketonuria or PKU has an important place in medical history as the first congenital metabolic disorder. It is a genetic defect in the phenylalanine hydroxylase enzyme existing in the liver and kidneys which is responsible for the conversion of phenylalanine to tyrosine. Deficiency of the enzyme results in accumulation of phenylalanine and its metabolites in the blood and other tissues. If left untreated, mental retardation, speech delays, eczema, seizures, behavioral abnormalities, etc would be expected. In PKU, proper nutrition is the only treatment of choice to prevent complications. The treatment is based on a low-protein diet, and elimination of all protein-rich foods to prevent severe mental retardation. Dietary changes in PKU are permanent through the life. By controlling the diet, we reach disease control too. The metabolic control in childhood and adolescence is related to patients' quality of life, and their mental status. Even in patients who resume treatment after a period of free diet, an enhancement in the quality of life is observed correlated with the phenylalanine level, in a way that when the phenylalanine level is between 2 and 6 mg/dL, the patients would have a higher quality of life. Moreover, the higher the patients' phenylalanine level, the lower the quality of life scores. Similarly, phenylalanine levels are associated with patients' social skills. The lower is the patients' phenylalanine level, the higher would be the social skills.

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Introduction

Definition of Phenylketonuria

Phenylketonuria, or PKU, has an important place in medical history as the first congenital metabolic disorder (1). It is caused by a genetic defect in the phenylalanine hydroxylase enzyme, which is mainly present in the liver and to some extent in the kidneys and is responsible for the conversion of phenylalanine to tyrosine. Deficiency of phenylalanine hydroxylase activity results in accumulation of phenylalanine and its metabolites in the blood and other tissues (2). In these children, due to the lack or insufficient activity of the enzyme, the amino acid phenylalanine is not converted to tyrosine or a small amount of conversion occurs (2).

As a result, the amino acid phenylalanine levels rise abnormally in the blood and is converted to other toxic substances that can affect the central nervous

system and disrupt the normal functions of the brain. If the disease is left untreated, brain damage and mental retardation would occur in the patient. Phenylalanine can be found in all protein foods. In healthy people, the normal level of this amino acid in the blood is low (1-2 mg/dL), but in PKU patients, it can reach up to 20 mg/dL, depending on the severity of the disease (2).

The severity of the disease varies from mild to severe, and the treatment is different for child to child. Its extreme type is known as the classic PKU. If it is left untreated; mental retardation, delayed speech, eczema, seizures, behavioral abnormalities, etc. would occur (2). patients with PKU have difficulty in communication, sustainable marriage and becoming independent from the femily. They also have problems in education and work in the general population compared to their healthy peers (3).

Prevalence of PKU in Iran and Worldwide

There is a wide variation in the incidence of the disease in different races, with the highest prevalence in Native Americans and Whites and the least prevalence in Blacks, Hispanics and Asians (3). On average, one out of every 1,500 US newborns is delivered with PKU. In total, approximately one out of every 48,000 babies born, suffers from PKU (3). There are few studies on the prevalence of phenylketonuria in Iran. In the national neonatal screening program on 630000 infants, the incidence rate of PKU was estimated to be 1 in 8000 (4). The prevalence of PKU in a study by Kabiri et al., in Tehran, 1 in 8,000 was reported (5). In the study of Golbahar et al. in Shiraz, it was reported to be 1 in 3,672 (6), and in the study of Habib et al. in Shiraz, Fars province, it was 1.6 in 10,000 (7). The researchers in Isfahan also found that out of 1,611 patients with retardation, 36 subjects (2%) sufferered from PKU (8).

PKU Control

In patients with PKU, the only available treatment to prevent the complications is proper nutrition. The treatment of these patients is based on a low-protein diet, and elimination of all protein-rich foods to prevent severe mental retardation (9). The goal of nutrition therapy in PKU is to reduce and maintain blood phenylalanine levels between 2 and 6 mg/dL throughout life, and to maintain normal tyrosine levels, to promote normal growth and development, and health (10).

Assessment of ntritional status in PKU patients is performed using the following information: (i) Patient history (history of treatment or interventions, reviewing family history, and socioeconomic status), (ii) Anthropometric indices (height, weight, head circumference, and body mass index (BMI)), (iii) Nutrition-related physical findings (muscle strength, an abnormal odor of urine and sweat, clinical manifestations of skin and hair, constipation, diarrhea, and vomiting) (10)

PKU patients have lifelong dietary changes. Patients who are treated with appropriate metabolic control from the first weeks of life and then lose this control later in childhood and adulthood, may experience irreversible neurological complications. On the other hand, in adults with phenylalanine hydroxylase deficiency, who have been diagnosed late and are severely mentally disabled, there has been a relative improvement in their status by lowering the blood phenylalanine levels. However, diet therapy is complex and costly and difficult to maintain in the long term. Optimizing and adjusting the diet as well as complementary therapies have had successful results in the treatment of some patients with the disease (1, 11-15).

Quality of Life in PKU Patients

Quality of life is the perception of each person about their health status and their satisfaction with it. The World Health Organization (WHO) recognizes a person's quality of life in the context of the cultural system and the values in which he or she lives, which is related to his or her goals, expectations, standards and concerns. It has two aspects including body and mental health. Optimal metabolic control following early and strict dietary treatment, especially during childhood and adolescence, may guarantee the health-related quality of life and mental health (16).

Diet control can lead to disease control too. This metabolic control during childhood and adolescence is correlated with the patients' quality of life and their mental status. Even in patients who have resumed treatment after a period of free diet, improvements in their quality of life scores can be noted. Problems such as depression and anxiety have been reported in patients who discontinued their phenylalanine restricted diet. If these patients follow a restricted diet of phenylalanine, a low blood phenylalanine concentration would be achieved; as well as an improvement in their quality of life criteria is found based on the quality of life questionnaire. In addition to diet, socioeconomic factors also are correlated with patients' quality of life and communication problems (1, 3, 11-18).

Association of Quality of Life and Diet in PKU Patients

Generally, PKU has a negative impact on the patients' quality of life. When the patient's

phenylalanine level is in the normal range, the patient has a sense of happiness and self-satisfaction. Besides, when the patient's phenylalanine level is in the abnormal range, the patient has anxiety, panic, and a depressed mood. Evasimon et al. found that in the PKU patient group, the quality of life was lower in comparison to the control group (3). Studies have shown that PKU patients have poor cognitive function and are weaker in social skills than their peers (19). They also have poor control over their social status. These patients generally tend to be less independent and more dependent on their parents (3).

In PKU patients, the quality of cognitive function has a negative correlation with their recent phenylalanine level. The higher the phenylalanine level, the lower the cognitive function. Studies have shown that when phenylalanine levels were between 0 and 7 mg/dL, social skills were demonstrated to be good (19). On the other hand, Cazzoric et al. showed that the score of quality of life was normal in mild and classic PKU patients with a phenylalanine level of 2 to 6 mg/dL. But the score was slightly higher in mild PKU patients treated with BH4 compared to classic PKU patients treated with diet. Also, the score of quality of life was higher in patients who were under treatment for a long period (20).

PKU patients face many problems in their social lives due to their adherence to their diet and use of special formulas. Their problems include a lack of independency and dependence on their parents. The patients who follow their diet and also use BH4 have a better quality of life. Bosch et al. showed the emotional effects of PKU, such as anxiety about blood phenylalanine levels, feeling guilty about not adhering to dietary restrictions, or receiving phenylalanine-free formula and anxiety about phenylalanine levels during pregnancy, these all affect one's quality of life (21).

However, after starting a phenylalanine restricted diet, these patients are in a better health status, which is usually associated with decreased anxiety, increased attention and concentration. They also have a better feeling about themselves and care more about themselves. In these patients, there was less aggression compared to pre-diet time. In general, the quality of life was higher in patients starting a phenylalanine restricted diet, compared to those who did not have a diet (15, 22).

Also, the quality of life in PKU patients was affected by their socioeconomic status. Patients with a better socioeconomic status had a higher quality of life. Also, the level of parents education was related to the quality of life of patients with PKU. Hatami et al. showed that thr scores of quality of life were significantly affected by the patients' educational level. Also, patients who received more training in this area had a higher quality of life (23).

There was also an association between parental occupational status and the patients' blood phenylalanine level, which may affect their quality of life (24). On the other hand, parental literacy status affected the quality of life of these patients, especially, maternal literacy and education. The lower the level of maternal education, the higher the amount of phenylalanine intake in patients as well as the lower quality of life in children or adolescents with PKU (11, 25).

Conclusion

The quality of life of PKU patients is related to their phenylalanine level, so that when the phenylalanine level is between 2 and 6 mg/dL, the patients have a higher quality of life score. The higher is the patients' phenylalanine level, the lower is their quality of life score. Similarly, phenylalanine levels are correlated with the patients' social skills. The lower is the patients' phenylalanine levels (in the range of 2 to 6 mg/dL), the higher is their social skills. Furthermore, the quality of life of these patients is reduced due to some problems regarding their dietary restrictions. Also, sociodemographic factors such as parents literacy and occupational status affects patients quality of life.

Conflict of Interest

None declared.

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