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The Importance, Contribution and Problems of Parents with Phenylketonuria (PKU) - An Association in İstanbul

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Abstract

Nutritional therapy and adaptation to this treatment are essential in Phenylketonuria (PKU), a congenital metabolic disease. This study was undertaken to determine the contribution of families in coping with problems that make nutritional adaptation difficult.

Difficulties faced by families in achieving low-protein, low-phenylalanine-containing products that are inadequate and expensive to achieve proper nutrition in PKU disease, the ways to cope with these difficulties, the problems that can be or are experienced in harmony with the environment of the patients, and the ways to cope with them consists the subject of the study.

As a result of the study it is understood that it is necessary and important to educate the families, to prevent the marriage of the relatives and to raise the awareness of the community in order not to increase the prevalence of recessive diseases in general frame. In the private area, the support of the family, the care to be shown about the nutrition, the minimization of the negative effects of the environment, the self-confidence to be given to the patient can create cognitive health and a life without any problems.

Keywords: Phenylketonuria, PKU, rare disorder, family, nutrition

1. Introduction

Phenylketonuria (PKU)

Phenylketonuria (PKU) definition of the Ministry of Health of the Republic of Turkey is as follows; PKU is a hereditary, metabolic disease. Phenylalanine, a protein building block, cannot be metabolized, accumulates in the blood and creates irreversible brain damage. If it is not identified and treated early, it inevitably results in severe mental retardation (Ana Çocuk Sağlığı Aile Planlaması Genel Müdürlüğü, 2016).

A similar definition was made by Köksal and Gökmen. PKU, known as a hereditary metabolic disease, where the essential amino acid phenylalanine cannot be metabolized to tyrosine due to lack or inadequacy of phenylalanine hydroxylase enzyme secreted from the liver, where the phenylalanine accumulated in the blood causes brain damage and urinary excretion of residual products such as phenyl pyruvic acid, phenyl lactic acid.

In the world, it is stated that on average, one out of every 50 people is a carrier, but the probability that two carriers will come together is 1: 2500 (Web- 1, 2016).

In the parents of individuals with PKU, there are two genes that are responsible for the production of phenylalanine hydroxylase enzyme, one that is solid and one that is defective and it has been explained that the child who got the bad genes from both parents born as PKU patient, the ones who got only one of the bad genes as the carrier like the mother and father born as carriers, and the child who only got the healthy genes born completely healthy. The likelihood of the carrier mother and father's giving birth to a sick child is as high as 25% (Köksal & Gökmen, 2015).

Background

PKU disease was discovered by Asbjorn Folling in 1934 as the result of research into two mentally retarded children. Folling accepted that phenyl pyruvic acid, a metabolite of the essential amino acid of phenylalanine, is a phenylalanine metabolism disorder in these two children after it has been identified as the metabolite. Later, it was demonstrated that phenylalanine hydroxylase activity, the enzyme that translates phenylalanine to tyrosine in the liver, with the accumulation of phenylalanine in the blood and spinal fluid of individuals with urinary phenyl pyruvic acid and mental retardation, has not been shown (Köksal & Gökmen, 2015).

After all these determinations, Lionel Penrose, a mental retardation specialist and a geneticist in August 1935, noticed that PKU was the first form of mental retardation, continued to study, about 10 years later Dr. Horst Bickel has shown that a diet that can prevent mental retardation, a complication of PKU disease (Scriver, 1995).

According to Blau et al., until the 1960s, most children born with PKU were totally mentally handicapped and spent most of their lives in treatment centers. In the 1960s, Robert Guthrie developed a diagnostic test for the PKU. This is a screening test, known as the Guthrie Test, made with newborn heel blood (Blau, J van Spronsen, & Lavy, Phenylketonuria, 2010).

The blood sample for newborn should ideally be taken on the next 3-5 days after birth. Breastfeeding the baby before blood is taken is important for the diagnosis of PKU. Thus, the metabolic development that will take place after phenylalanine, which the baby takes, will be observed.

The original, semi-quantitative test known as the Guthrie test is based on a bacterial inhibition assay, making mass screening simple, cheap and very cost-effective. Gradually (but not entirely) it was replaced by newer methods, such as chromatography, fluorimeter and more recently tandem mass spectrometry. Guthrie's landmark discovery and implementation of the first newborn screening programs for PKU could be – in a 50 year retrospective – easily considered as one of the greatest advances in medicine (Groselja, Tanseka, & Battelin, 2014).

There are different sources of information on the prevalence of PKU in the world. In a study conducted in 2008, the incidence of PKU was 1: 200,000 in Finland, 1: 125,000 in Japan, 1: 7.000 in Czechoslovakia, and 1: 2.600 in Turkey. The high incidence of PKU in Turkey is due to the widespread marriage of relatives and the low incidence in Finland and Japan is explained by the 'negative founder effect' in Finland and in Japan by genetic drift in the formation of the island population. Negative founder effect is an effect created by the fact that the current population of Finland is the result of the expansion of a very small population established up to 2000 years ago, and that there was little migration in this process (Williams , Mamotte , & Burnett , 2008).

In another source there are prevalence data for PKU. In Europe, the prevalence is about 1/10.000 livebirths but 1/4000 births in Turkey because of high consanguinity within the population. Finland has the lowest prevalence in Europe with 1/100 000. In the USA the prevalence is 1/ 15 000 but it varies from about 1/ 50 000 to 1/25 000 births for Latin America (Blau & ark, Phenylketonuria, 2010).

In Hacettepe Screening Center, one of the most important screening centers in Turkey, 383 out of 1,605,582 babies screened by the Guthrie test were found to have hyper phenylalanine (very close to 1 in 4000) (Ozalp & ark, 2001). This data is consistent with the information provided by Blau et al. (2010).

In a study on consanguineous marriages in Turkey, the region where the majority of the marriages were observed was identified as Eastern Anatolia Region with the ratio of 33%. This is followed by the Black Sea Region with 32.6%. In the Aegean Region this ratio is found to be 1.4% (Tabak, 2008).

In a study that proved the efficacy of consanguineous marriages in the formation of genetic diseases, in Western Black Sea Region, the incidence of chronic and genetic diseases consisting as a result of consanguineous marriages was examined, 320 women, 218 of whom had consanguineous marriages, participated in the study. The rate of genetic disease incidence was 10.7% among children of consanguineous marriages, while the incidence of genetic diseases among children of non-consanguineous families was 3.7% (Arslan, 2010).

2. Materials and Methods

This study was conducted in PKU Family Association in İstanbul, Turkey. In the study in–depth interviews were conducted with 6 mothers who are member of association and who has child with PKU. One of the interviewers is the President of the Association and the others are volunteers working in the association, and in the cafés, which produce PKU-suitable products, belonging to the association.

The first appointment was in November 2016. These conversations continued until the beginning of April 2017. In every meeting, the aim of the study was explained, the

permission was taken every time from the participants to make audio recording. The in-depth interviews started with the intention to learn the relationship of nutrition and PKU.

The study which will search the disease's relationship with the nourishment, as the participants are the mothers of PKU patients, has turned into an emphasis on the contribution of parents to the lives of PKU patients. Because of the information that changed the direction of the work, the literature studies were re-established and new resources were found in this direction.

The anthropological assessment was carried out by analyzing the interviews and the information obtained from the literature sources together. Statistical evaluation was not made in this study. The codename of the participants (M1, M2, P1, etc.) was written on the headline of the excerpts taken from the interview. The real identities were not used.

3. Results and Discussion

In PKU, a disease in which the enzyme phenylalanine hydroxylase does not work or underworks, and therefore requires a limited phenylalanine lifetime, patients have to take a lifelong control level of phenylalanine and have a diet to live well and not to lose their intelligence.

PKU dietary therapy is based on keeping blood phenylalanine levels at safe intervals, limiting this amino acid and relieving the patient's need for tyrosine.

Nutritional therapy in each disease is specific to the patient, but PKU is vitally important for each gram of food, so the variety and quantity should be tailored to and specific to the patient's wishes at the limit that will not exceed the allowable limits.

Just making a diet is not enough, the appropriateness of the diet needs to be checked at certain intervals. For this purpose, according to the application rules in Turkey, it is necessary to perform phenylalanine control for the newborn 2 times a week for the first 6 months, one time a week for 6 months to 1 year old babies, and once in 10 days after the first year of the baby. These control intervals can vary according to the condition of the patient under the doctor's control. M1 told the following about her 21-year-old daughter who is studying 'Latin Language and Literature' at the university;

> M1 - I take my daughter once a month to ÇAPA Medical Faculty of Istanbul University according to the control interval determined by her doctors. When we think that the number of patients with PKU in our country is higher than other countries, there are insufficient number of health personnel who are dealing with congenital metabolic diseases and there is only one dietitian in the hospital. Also, we cannot see a dietitian without the doctor's request. There are a lot of patients, health care providers are few and so the time being interviewed is also limited.

The fact that the PKU, a rare disease, is not well known in the society, the lack of care and support, upset the parent and emphasizes the importance of early recognition.

> M5- Let's just say that baby's heel blood was taken, values are within limits. That kid is just being followed, not being taken on a diet. Fever, vaccines are being followed. Then, we switch to supplementary food. 1-2 years pass, values increase. That kid tastes meat, milk, eggs, cheese until then and maybe he likes it. In that case, starting a diet is very difficult for both the family and the child. They are fighting a great deal to be able to adapt to that diet. But in early diagnosis, he doesn't know their tastes, he only recognizes the food that he is able to eat. As his palate develops accordingly, there is no problem.

There are cases that arise at older ages that are not understood because of their low values. For example, she lives without being aware for 23 years, but suddenly she is faced with this diagnosis because the tolerance of the enzyme system is over. A new and difficult life is beginning for her. There is a story of a blonde girl, which hurts our hearts. Her perception is a little low but they do not suspect and accept her as 'dumb blonde'. However, as she has severe pain, she goes to many doctors and finally gets diagnosed. If not diagnosed, this disease may lead to her death. This is the worst scenario.

> M2- We are deemed fortunate that our children are diagnosed early. If she was diagnosed at the age of 5 then she would have a different situation. We would have had to forbid the food that she had tasted. She would have learned the concept of 'Craving'. When they are diagnosed early, they do not crave for anything because they open their eyes with PKU when they are born. We never told my daughter that she is sick. We have been teaching the diet since the infancy by saying that you should eat them to be healthy.

According to the information given by the association, Istanbul University ÇAPA Faculty of Medicine and the PKU Family Association are very helpful in terms of patients and their families. Thus, families, whose child has just been diagnosed, who feel bad and do not know what to do, meet with other families who are experienced in PKU in the association, they are relaxed and motivated when they learn that they are older PKU patients who have not experienced mental retardation.
M3, who has a son with PKU at the age of 2, tells us that he did not get much benefit from the hospital and that she came here because she was directed to the Association;

> M3 - After they diagnosed, and informed us about the disease, and the diets were told, they led us here. I came here because I did not know what to do.

In the PKU cafeteria working within the association, the details of the diet are discussed and the food, desserts, which children can eat, are taught; the options that can be offered are increased and diversity can be provided. From time to time PKU Recipe Days are organized and various cakes, pastries, cookies are made, and recipes used for special products are taught.

This mentioned case study is valid for İstanbul. The association can send the products to the requesters far away from the place. They also send the products to the families with low income levels, but considering the whole Turkey it can be said that this service is not enough.
Regarding the records and the prevalence of PKU disease in Turkey, the President of the Association says:

> President of the Association - There is no record in the Ministry of Health until 1993. Heel scanning becomes mandatory after 1993. But mothers do not know what that will do. We have reliable records since 2006. According to records for 11 years, the most widespread region is Central Anatolia. Then Black Sea Region, and then South East Region. The most important reason is consanguineous marriage. Parishes are seem to be common in Central Anatolia. The live in closed communities.

Whereas in Tabak's study, the eastern Anatolia region appears to be the region where consanguineous marriages are most prevalent. M1 joins at this point by adding the following;

> M1: Children who are not born in the hospital are not receiving heel blood test and the disease cannot be detected. The child does not have a special diet and after a while he suffers a seizure and dies. He dies without knowing that he has PKU. They say, 'God gave him but God take him back'. When we look at the East Region of Anatolia, Southeast Region of Anatolia, there seems to be a lot of consanguineous marriages, but no PKU record.

It is understood that there is a vicious cycle; the low level of development in the areas where consanguineous marriages are made has a low income level and that there is no possibility of obtaining food and special products for the treatment of PKU children.
If a child is PKU, does the family who has married a relative give birth to a child again? The information that the President of the Association gave us was surprising;

> President of the Association - We warn parents who are carriers. We say that both of you are carriers, so the baby has a chance to be PKU at the ratio of 25%. They say, so we can have 3 more children, one in 4 can be PKU and the others won't be. They're almost like gambling. They encourage each other by saying, 'I have an acquaintance, he married to his uncle's daughter, they had 3 children and the children are so healthy'.

According to interviews with the PKU Family Association, there are clogged roads that will make it easier to deal with the disease due to financial problems. Due to the fact that special products are not produced for PKU patients in our country, because imported products are obliged to be imported, the foods that may be much more suitable are offered for sale at a level that will force the family's budgets. It is stated that PKU families in Turkey are having difficulty in getting special foods with prices as high as 10-20 times compared to the prices of

normal foods. To overcome these problems, related with a meeting on cooperation with the association industry, M2 said;

> M2 - Big firms do not want to do boutique production. For example, if we think about milk, they do not want to open a special line and produce low-protein milk. And the imported ones are not always found. Since sales of imported products are realized within the scope of the social project, the grocery stores do not charge a rayon fee when they put these products in the rayon. So, they do not want to give these products a big rayon. Instead, they can put another product on the rayon and earn money. That's why, they get few products and give them a small rayon, and there are few products, it is sold out so fast.

The amount of state aid that is learned through the interview is really amazing. In the age range of 0-5 years, PKU patient can receive 70 TL / month as the state aid, it is 116 TL / month for 5-15 years old and 120 TL / month for adults over 15 years old. In the past years, the aid of the state was sent to the family as macaroni and flour, but in the recent period only money was given to help.

Financial problems, having few PKU nutritional products, these products' being expensive and being few in variety are the concrete problems that patients face. Besides this concrete fact, it is not possible to ignore the positive and negative feelings of the patients, their families and their relatives. Already in the literature there are many researches about this subject.

In a study that examined the effect of high phenylalanine levels on the mood and neuropsychological functions of individuals with PKU, it was concluded that high phenylalanine levels had a direct negative effect on attention and emotional state. High phenylalanine has been shown to reduce tryptophan and serotonin levels, and a reduction in serotonin levels has been implicated in the pathogenesis of psychological disorders, including depression (Amber & ark, 2010).

From Amber's work; it is understood that the origin of the psychological findings explained by physiology in these patients is the nature of the PKU disease.

The neurologically negative emotional state of PKU patients, as well as the negative, exclusionary, judicial attitude of the external environment, affect the social lives of the patients. M2, with a 21-year-old daughter with PKU, tells what she does for protection from these:

> M2- I was always warning the people around me. My neighbors, my relatives. P2 has this situation, she has special food, and anything you offer can harm her. If you are considering her goodness, please do not give her anything except water without my knowledge.

One of the most important consequences of an anthropological dissertation study has been the differentiation of patients due to the obligation to make a special diet. Therefore, it is concluded that the feeling of exclusion by the society affects the family and the patient's perceptions negatively (Burgut, 2014).

It is understood that life for the person with PKU and his family must always be controlled. It should be difficult not only for parents but also for siblings. M3 tells what a family with twin's lives;

> M3- One of the children has PKU, the other does not. Mother was having a hard time, and she used to wish they both had PKU, or both didn't, it was very difficult for her. One day, she cooked meatballs for Uzay. And they found him eating the meatballs in her mother's bedroom, behind the door, so that his twin sister Duygu, would not smell and want to eat it. Their mother got so sad, but anyway they're grown up now, are going to college. In another family there are two siblings with two year gap among them. The healthy one would always complain that his brother with PKU always had special food prepared for him. He is jealous. So every family is experiencing different situations.

From the mothers we talked at the association, M1 says that some families lock the refrigerator, eat when the child is sleeping, or eat before their child comes home. As no one will care this much outside, she thinks that if her child learns coping with this problem, her child can be stronger outside. She tells that she pushed her daughter into society early so that she can live without being excluded by the society;

> M1 - I gave my daughter to the nursery school at the age of two. I wanted her to learn to say 'no'. 'No, I don't eat it', 'No, No, No...' So, I wanted her to say 'no' as soon as earlier. I never said her 'forbidden'. 'You can eat it if you want, but after you have eaten a few times, you won't be able to understand me when I say, 'honey, can you get me some water?' or 'Can you turn the lights off?'. If you continue to eat, one day, you won't be able to react to me when I say something to you. Because your body and your brain will be harmed badly. If you want to do harm yourself, you can eat what we eat'.

M5 says only mother support is not enough. When the mother says no, the father will not say yes, and vice versa, when the father says no, the mother will not give her the forbidden food. She says both should be solid and exact.

> M5 - I keep people in my life who will make our life easier. I totally wrote off the ones who made our life harder. We should definitely pick them out. Our children also choose their friends like this. They created a friend circle who will not exclude, question or make their status a problem.

PKU is also required to make a special diet as it is in the majority of other congenital metabolic diseases. It is necessary to raise awareness of healthy people from the age of childhood, to help the patients to do not feel different, who need to consume the special product. The suggestion is as follows;

> President of the Association - Especially if there are students who will consume special products in the class or school of primary and secondary school children, it will be useful in the long term to inform

> the other friends about the illness by their teachers, to explain the necessity to respect this situation and to raise awareness of the children.

M4, with an 8-year-old son with PKU, working in the association, said:

> M4 - As PKU children do not have meat products such as meatballs and poultry, their friends can interpret them as poor and penniless. People who cannot compete with the outside feel better with their friends and family since they are more understanding.

M2 says there are children who do not want to take photographs at the organization events, who do not want their name known, and who keep the situation as a secret in their school. They do not tell their friends they have PKU. When they go out with their friends, they drink a cup of tea saying that they are full and will not eat anything. Indeed, they make their own lives miserable. She says about her own daughter who is 21 years old;

> M2 - When her friends go to a restaurant where she can eat something, she becomes happy, even when her friends chooses the same menu as her, for example salad, my daughter becomes happier.

Adults with PKU also want to behave as the majority, and as the patients grow up and have the chance to get in social life, they keep their diseases as a secret not to seem different, for example, if they go for a dinner, they say that they are full and only drink water or tea. Sometimes the special products and limited diet that are not worried about at a young age can get more difficult as they grow.

Many different situations were told when considered what the families first reactions were when they learned their children had PKU diagnosis and what they lived during the acceptance process. Each family's ways of coping with can be different. The only thing that is common is that when families accept the situation and manage this very difficult process in a healthy way, there are no dramatic consequences and healthy, professional, socialized individuals can be grown up.

> M1 – The process very difficult. I've fought for a year and a half with it. The families initially refuse the disease and spend the majority of their time asking ‘Why is my child?’ And after a period of sadness, they feel better, and they enter into a process of dealing with, coping with the disease when they believe their children will grow up healthy without any complications from diet therapy.

Even if diet is difficult and hard to follow, if the diet is well understood and strictly adhered to the treatment, complications will be minimized and a healthy life can be maintained without mental retardation.

As PKU disease is innate, the fact that the age of the individual is so young in the process of accepting and adapting to the disease makes them absolutely dependent on family support in every respect. Given the fact that consanguineous marriages increase the incidence of illness,

there is a vicious cycle of confrontation here when the education level of the parents is taken into consideration.

According to Ozalp et al. (2001) PKU screening study, there are two main reasons why individuals cannot adapt to diet treatment; The lack of social insurance for some of the families, the inability to receive treatment and the absence of state aid for this reason, and the uneducated and unconscious nature of the family.

In Poland, a study was conducted with 53 patients with PKU who were unable to comply with dietary therapy to find out the causes of malfunctions in nutritional therapy. In the study, the main problems experienced by discordant individuals are; the inadequacy of the business environment to the disease, the high cost of the low protein special products and the inadequate knowledge of the patients on the diet (Bik & ark, 2009).

In another study, the reasons, in a intertwined and co-existing way, for not being able to comply with the diet are as follows; being ashamed of the diet while in the social community at 90%, low family dependency at 83.8%, difficulty in preparing food at 78.9%, low socioeconomic status at 76.7%, lack of social insurance to buy drugs and low-protein foods, formulas at 64.4%, and not adapting to the role models such as teachers, consultants, caretakers at 61.1% (Bernstein & ark, 2013).

Considering that this is the rate of embarrassment from the private diet while in the social community, it is also necessary to understand how difficult it is for individuals with PKU to find a suitable menu in restaurants. M3 says that apart from the proper menu, the repulsive warnings for them made them disgusting.

> M3 - In most places there are signs like 'It is forbidden to bring food, beverage from the outside!' PKU patients are in a difficult situation when there are staff or restaurants that do not understand the special situation. At least, we should be able to enter restaurants with our specially prepared breads for our own diet. In order to avoid such negative approaches, we use slogans like 'Respect to my diet!' in our events.

It is thought that individuals with PKU who have to constantly have a limited diet can feel themselves excluded from society, have difficulty in strengthening their social ties and establishing interpersonal relationships, because eating and drinking is no longer a vital necessity but a social necessity in human life. However, some studies have shown that PKU may not be a disappointing disease, even there may be multiple reasons why patients may feel lucky. For example, in a study in 2011 carried out to share the experiences of PKU patients in Norway, In-depth interviews were conducted with 11 adult patients, aged 20-30, and participants were shown positive thoughts on their own health beyond reality. It is concluded that the individuals with PKU feel lucky because they have families who can manage this disease with diets, grateful because of the place they were born and live, and good because they have the opportunities to get sufficient knowledge and treatment (Diesen & Counsel, 2016).

4. Conclusion

It is understood that there is not enough level of consciousness in society yet about the disease of PKU. In order to cope with this disease, which is closely related to consanguineous marriages, the level of education needs to be increased first. It should be ensured that families

are more caring about the special situations that the disease requires, teachers and instructors should be more informed and aware about the exclusion behavior. There is also a need to create awareness of special products in food service systems outside home.

In addition to increasing education and training in this disease where treatment problems are frequently encountered due to financial problems, the assistance of the government will also contribute considerably. In this case, what is thought to be a better aid than money is to encourage the main food firms to produce special foods for PKU patients. So, it is thought that the access to special food will increase and the financial problems to reach the products will decrease.

It is understood that, in the private area, the support of the family in terms of nutrition is the most important element. It can be said that a problem-free life and cognitive health is possible if the adverse effects of the environment are minimized and the family is committed to feed with the right products.

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