PHENYLALANINE RESTRICTED DIET TREATMENT OF THE AGGRESSIVE BEHAVIOURS OF A PERSON WITH MENTAL RETARDATION

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Introduction

Phenylketonuria is a genetic abnormality that triggers an incapacity to metabolise phenylalanine (Phe), an amino acid present in nutritional proteins. This incapacity leads to an accumulation of Phe and its by-products in the blood and tissues, which drastically compromises the neurological and intellectual development of a person (Pueschel, 1996). Following the establishment of national and state screening programmes (circa 1965), phenylketonuria has ceased to be a cause of mental retardation for the vast majority of persons affected by this incapacity. With the possibility of detection at birth and the immediate introduction of a Phe-restricted diet, development can progress at normal rates (Koch et al., 1996). However, individuals with phenylketonuria who were born before the development of these screening programmes and early interventions have, unfortunately, developed mental retardation.

It is clear that the harmful effects of a high Phe blood level during the first years of life are largely irreversible, especially where intellectual development is concerned (Bruhl et al., 1965). However, certain toxic effects manifested in problem behaviours seem to be reversible, even in adults with phenylketonuria who have followed a regular diet throughout their entire lives.
An improvement in behaviour is sometimes noted when these adults are given a special diet to reduce their Phe blood levels (Harper and Reid, 1987; Hoskin et al., 1992). However, the introduction of a Phe-restricted diet to reduce problem behaviours remains controversial possibly because of three types of methodological difficulties in past studies.

First, the length of time during which the special diet has been implemented varies considerably from one study to another and may be a cause of inconsistencies in the results reported. Only two studies were found in the literature that used an experimental design to investigate the impact of diet on problem behaviours. In both studies, the effect of diet was evaluated by alternating two-week periods of regular and Phe-restricted diets (Hambraeus et al., 1971; Marholin et al., 1978). The results did not show any effect of the Phe-restricted diet on behaviour. On the other hand, in two case studies where a diet was maintained for several months, positive effects on behaviour were detectable a month and a half after its introduction (Harper and Reid, 1987; Hoskin et al., 1992). Given that clinical experience suggests that the diet must be maintained for at least six months before a decision can be made regarding its effectiveness for any given patient (Personal communication, Ryan, S., 1999), the conclusions drawn from the two experimental studies above may be misleading. That is, the absence of an impact of diet on behaviour may have been due to interventions that were carried out for an inadequate time period.

Second, the presence of positive effects resulting from a Phe-restricted diet seems to depend on the type of behaviour problems manifested by a person. Indeed, the introduction of such a diet has little positive impact for persons whose main difficulties are a high frequency of stereotyped behaviours (Brunner et al., 1987; Marholin et al., 1978; Thompson, 1995). Positive effects are often observed, however, when patients present difficulties characterised by agitation and aggressive conduct (Harper and Reid, 1987; Hoskin et al., 1992; Williams, 1998). Thus, the nature of the behaviour problems must be taken into consideration in order to draw valid conclusions about the efficacy of the diet.

Third, a Phe-restricted diet can be poorly tolerated. Indeed, it may case vomiting (Brunner et al., 1987), an increase in Phe blood level (Marholin et al., 1978) and, in some cases, an exacerbation of the side effects of medication (Harvey and Kirk, 1995). Given these potential negative effects, the diet must be planned carefully and interdisciplinary follow-up must be ensured. It should be noted that, in general, these negative side effects are relatively benign and completely reversible by diet modifications or by the resumption of a regular diet. Thus, there are no major impediments to completing a trial of a Phe-restricted diet as long as adequate follow-up is ensured.

A more comprehensive evaluation of the diet’s effects on aggressive behaviours is needed given the challenge of dealing with these behaviours in the absence of efficient and unrestricted interventions (c.f. Pyles et al., 1997). Therefore, the objective of this single-case study was to evaluate the extent to which a Phe-restricted diet, assiduously followed during a long period of time, would lead to a reduction of aggressive behaviours in an individual with mental retardation who lived in an institution for more than thirty years. Furthermore, the dosage of prescribed medication used to control the patient’s aggressive behaviours was modified as a function of the efficacy of the diet.
Method

Participant

The female participant began to display developmental problems at an early age. She was diagnosed with phenylketonuria at the age of two. A Phe-restricted diet was prescribed at the age of seven but, unfortunately, it could not be sustained in her family environment. At the age of eight, the patient received a diagnosis of profound mental retardation. She was admitted to a psychiatric institution at the age of eleven and has permanently resided in this milieu since. The patient was 41 years old at the beginning of the study. She did not communicate verbally and showed classical phenylketonuria symptoms.

The patient had been living in the unit where the present study was performed for several months. The reason for her transfer was the severity of her behavioural problems. During frequent periods of agitation, she would scream in an intense and repetitive manner, knock down objects and attack treatment team members or other patients. During these crises, the severity of her distress was reflected in her facial expressions. She also displayed other problem behaviours such as pica and self-mutilation. No functional relation between her problem behaviours and environmental events could be identified. According to past psychiatric records, she had displayed severe problem behaviours for about 30 years. Past pharmacological and behavioural treatments had shown little or no efficacy.

Research protocol

The diet aims to reduce the patient’s Phe blood level to one that is comparable to that of an adult with phenylketonuria who has assiduously followed a Phe-restricted diet since birth. This level varies between 480 and 720 umol/litre and has been shown to be related to high levels of intellectual and social functioning for adults with phenylketonuria (Koch et al., 1996). In the context of the present study, the Phe content of the diet was initially established at 1000 mg per day and was then reduced to 900 mg after three months, thereby ensuring good control of Phe blood level. The diet essentially consists of fruits, vegetables and grain products. Special products low in Phe (e.g. bread, pasta, broth) were also used. An appropriate supply of Phe-free proteins and tyrosine was ensured by the consumption of special beverages. Tyrosine is an essential by-product of Phe.

The elaborated diet ensures a sufficient energy supply and, therefore, the metabolism of the patient did not have to draw on additional energy sources.
from tissue proteins. This was important because these proteins contain Phe and their use would have led to an increase of Phe blood level. Weight loss was used as an indicator of the use of these proteins. At the start of the diet, the patient’s weight was 43 kg. The energy supply was set at 10,500 kilojoules per day. Following gains in the patient’s weight during the first six months of the diet, the supply was reduced to 9,660 kilojoules per day, which stabilised her weight at approximately 50 kg.

Monthly blood tests were performed to monitor change in Phe blood level. A month before the diet was introduced, the patient’s Phe level was 1705 umol/litre which dropped to 772 umol/litre after a month of diet maintenance. With the exception of a relatively high level during the second and third months of the diet, the Phe level was adequately controlled, varying between 232 and 773 umol/litre. The patient tolerated the diet well, seemed to appreciate the food and did not show signs of anaemia.

Results

Number of hours spent in seclusion per week

Number of hours spent in seclusion is presented for both the baseline period and the treatment period in FIGURE 1. The baseline corresponds to the time period during which the patient followed a regular diet. This period began when the patient first arrived in the unit. The treatment period, which lasted 12 months, began with the introduction of the Phe-restricted diet.

During the first seven weeks of baseline, the number of hours spent in seclusion is small, probably due to her transfer to a new environment. In the course of the following weeks, seclusion increases considerably, reaching a maximum of 50 and 63 hours per week (weeks 16 and 17). This increase coincided with the occurrence and treatment of a vaginal yeast infection. Seclusion decreases to about 15 hours per week during the weeks immediately preceding the introduction of the Phe-restricted diet and rises to 27 hours per week. It remains high for about a month and then decreases markedly to almost nil for about six months (weeks 41 to 64) except for a brief burst at week 40. During the tenth month of the diet, a short-term increase in hours (weeks 65 to 68) coincides with the complete withdrawal of medication (see FIGURE 2) and the presence of flu symptoms. During the next month and a half (weeks 68 to 74), the number of hours spent in seclusion becomes nil once again and remains at this level until the end of the study period.

Medication

During the period preceding the introduction of the diet, the patient was given
FIGURE 1
Number of hours spent in seclusion with or without restraint as a function of type of diet

medication to control her agitation: 4 mg of Rivotril (clonazepan) and 150 mg of Largactil (chlorpromazine) each day. A gradual withdrawal of medication was initiated about 14 weeks (13 weeks for Rivotril and 15 weeks for Largactil) after the onset of treatment when the positive effects of the diet on the patient’s behaviour became obvious. Rivotril was completely withdrawn 6 months (week 46) after the start of the diet, followed by Largactil 4 months (week 62) later (FIGURE 2).

Other changes observed during the course of the diet

Other changes, notable from a clinical standpoint, were observed during the course of treatment and, although they were not formally assessed, they are nevertheless worth mentioning. Pica was no longer part of the patient’s behavioural repertoire. Furthermore, she showed a substantial improvement in mood, a change in facial expressions from distress to greater
FIGURE 2
Daily dosage of medication as a function of type of diet

Regular diet

Restricted diet

Weeks:
Largactil

Weeks:
Rivotril
well-being (i.e., she was smiling more often), and a cessation of screaming. Her constipation problem was also alleviated. Although she continued to show severe deficits in adaptive behaviours, her basic autonomy improved noticeably. After 10 months of the diet, toilet training was installed and she occasionally is permitted to leave the unit.

Discussion

The objective of this single-case study was to evaluate the efficacy of a Phe-restricted diet introduced to reduce the aggressive behaviours of a patient with a profound intellectual deficiency due to an untreated phenylketonuria. This diet reduced her Phe blood level to a level similar to that of adults who have been treated at an early age for this condition. The patient did not reject the new diet, did not lose any weight and did not experience vomiting. No complications were noted. Consequently, it was possible to maintain the diet during a one year period and to study its effects during that time.

Two limitations of this study can be raised. First, the frequency of severe aggressive behaviours was not specifically monitored through direct observation and therefore a description of the patient’s aggressive behaviours can not be provided. Nevertheless, the use of the number of hours spent in seclusion as an indicator of behaviour problems offers at least two advantages. First, the occurrence of aggressive behaviours could be measured for all of the patient’s waking hours rather than for a short time period that would have had to have been sampled through direct observation (e.g. Marholin et al., 1978). Furthermore, this indicator assesses the occurrence of aggressive behaviours that are clinically significant, that is, those that cannot be ignored or controlled in an unrestrictive manner. Thus, in spite of its descriptive limitations, the number of hours spent in seclusion represents a clinically valid indicator.

A second limitation concerns the timing of the introduction of the Phe-restricted diet which coincided closely with the treatment of a minor medical problem (i.e. a vaginal yeast infection). At first sight, the decrease of hours spent in seclusion could be attributed to the alleviation of this problem rather than to the introduction of the diet. However, an examination of the patient’s hospital records revealed that, in the past, she was consistently put in seclusion for an average of 15 hours per week and, she rarely spent more than two weeks without being secluded. Given these historical data, it is highly unlikely that the simple treatment of a minor medical problem would be the cause of such a striking improvement in the patient’s behaviour. Indeed, seclusion was reduced to only one hour during a six month period. Thus, the introduction of the Phe-restricted diet is the most plausible explanation for the pronounced decrease in the number of hours spent in seclusion during the course of the observed period.

It would be unrealistic to aim for the total elimination of the toxic effects of a high Phe blood level in non-treated adults, even if the special diet is maintained during several years (Bruhl et al., 1965). The complete extinction of problem behaviours might not even be a sustainable goal without the addition of complementary treatment strategies. The intense agitation of the patient during periods in which she developed minor health problems (i.e. a vaginal yeast infection or the flu) shows that she was, and continues to be, a vulnerable person even with the introduction of a diet. Nevertheless, compared to medication or restraint, the Phe-restricted diet re-
resents an efficient and unrestrictive manner to reduce agitation and aggressive behaviours. The decrease of hours spent in seclusion also probably represents a significant improvement in the patient’s quality of life (see Fisher, 1994). Finally, the effective control of the patient’s aggressive behaviours enabled the members of the treatment team to introduce re-education strategies aimed to improve her communication skills and to increase her basic autonomy. It would be interesting to evaluate the combined efficacy of a Phe-restricted diet and re-education strategies in future studies.

Footnote

1 An ABAB schema is one in which baseline (A) and treatment (B) periods are alternated twice. This would mean observing the patient during a regular diet period followed by a Phe-restricted diet one, another period of regular diet and a final Phe-restricted diet one.

Summary

This single case study examines the efficacy of a phenylalanine restricted diet introduced to reduce the severe aggressive behaviours of a female patient with mental retardation secondary to an untreated phenylketonuria. This diet is well accepted and permits an adequate control of phenylalanine blood level. The frequency of severe aggressive behaviours, as indexed by the number of hours spent in seclusion, showed an important decrease following the introduction of the diet, which then permitted the complete withdrawal of medication. The phenylalanine restricted diet seems to be an efficient and relatively unrestrictive intervention to reduce aggressive behaviour in individuals affected by untreated phenylketonuria. The complementary contribution of re-education strategies is discussed.

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