The implications of Phenylketonuria on oral health

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Abstract

Purpose: This study was performed to evaluate the oral health of children with PKU and to assess, in vitro, the erosive potential of 5 amino acid supplements commonly prescribed in the management of these children.

Methods: Forty children with phenylketonuria underwent a full dental examination and were compared with an age and sex matched control group. The erosive potential of the supplements was assessed by comparing their pH and titratable acidity to those of Coca Cola and orange juice.

Results: There was no significant difference between the affected and control groups in the level of dental caries, with over 75% of the children examined being caries-free. However, significantly more (33%) children with phenylketonuria exhibited signs of tooth wear compared with 24% of the controls (P < 0.05). While Coca Cola had the lowest pH (2.46), the titratable acidity of the flavoured supplements (92.86-126.8 mEq/l) was significantly higher than both their unflavored counterparts (4.18-14.0mEq/l) and Coca Cola (38.56mEq/l).

Conclusions: Despite the potentially damaging nature of their diet, significantly less children with PKU had ever seen a dentist. Health professionals involved in the care of these patients should be aware of the implications of management and provide appropriate dental advice and referral. (Pediatr Dent 21:433-437, 1999)

Phenylketonuria (PKU) is an autosomal recessive genetic disorder with a birth incidence of between 1:5,000 to 1:20,000.1 Individuals affected by this inborn error of metabolism have a deficiency in the liver enzyme phenylalanine hydroxylase, which converts phenylalanine to tyrosine. The resulting abnormally high concentration of plasma phenylalanine will, if not treated within the first few weeks of life, lead to progressive intellectual disability. With neonatal screening currently available in many countries, affected children are usually treated from early infancy; these children can grow and develop normally, and may be expected to lead a relatively normal, healthy life into adulthood.

The management of these patients involves adherence to a low protein diet, which is essential to restrict the intake of phenylalanine to only the amount necessary for normal protein synthesis. To make up the energy requirements, the diets of these children are often high in carbohydrates, which are usually taken frequently throughout the day. To ensure sufficient intake of essential amino acids, phenylalanine-free protein supplements (available in powder form to be made up as drinks) are necessary. These too are consumed at regular intervals throughout the day and occasionally during the night.

Dental caries is a multifactorial disease of bacterial origin. However, the role of fermentable carbohydrates in providing a substrate from which the cariogenic bacteria can produce acid, which in turn causes demineralization (and eventual cavitation) of susceptible tooth surfaces, is well recognized.2 Furthermore not only is the total amount of sugar consumed an important factor influencing the development of caries but also the frequency of intake, with increased snacking related to increased caries incidence.3,4 Erosion is the progressive loss of dental hard tissues not involving bacteria.5 Dental erosion has been attributed to the presence of acids in the mouth. The origin of these acids may be either extrinsic or intrinsic. Extrinsic acids are found principally in the diet in the form of acidic drinks and foods6 while intrinsic acids are found in the stomach contents and may be regurgitated back in to the mouth in gastric reflux or in certain eating disorders.7 Given the combination of the frequent intake of carbohydrates and the potentially acidic nature of the protein supplements, children with PKU are on a diet which appears to place them at risk of developing either or both dental caries and erosion. The potential sequelae to both dental caries and erosion is loss of tooth structure, cavities, pain, infection, need for extensive (and expensive) restorative dental treatment, and even dental extractions. To date there have been very few reports on oral health of children with PKU,8-10 These studies suggest that affected children do not experience significantly greater amounts of dental caries. To date, there has been no assessment of the potential problem of dental erosion in these children. The aims of this study were twofold; to evaluate the oral health of children with PKU and secondly to assess, in vitro, the erosive potential of the amino acid supplements taken by children with PKU.

Methods

Clinical study

Ethical approval was gained from the ethics committee at the New Children’s Hospital, Westmead, Sydney, Australia. The...
children involved in the study were among those who attended the PKU clinic held weekly at the hospital and whose parents had given written consent for their participation. A control group made up of unaffected siblings and healthy children enrolled from the general outpatient clinic waiting area was also examined. The age of the children ranged from two years and two months to 17 years and 10 months. A standard questionnaire was completed by all participating parents to establish information concerning their child’s oral hygiene practices, exposure to fluoride, and dental attendance history.

All children were examined in the dental chair, using overhead dental lighting, a mouth mirror, and a probe by one of the authors (H A). A full dental examination was carried out; caries diagnosis was based on the criteria set down by the World Health Organization, in which diagnosis was made only where there was a visible cavity involving dentine. Radiographs were not taken as part of the study protocol. If there was a clinical indication radiographs were arranged for a subsequent visit as part of routine dental care or the patient was referred to their general practitioner for care. Assessment of oral hygiene levels was done using Modified Plaque Index and Gingival Inflammation Index. The presence of tooth wear was recorded using the Tooth Wear Index of Smith and Knight. Intraoral photographs were taken for recording/scoring tooth wear and an assessment was made of whether the wear resembled dental erosion or had the appearance of tissue loss caused by other wear processes such as attrition or abrasion.

Statistical analysis was conducted using SPSS for Windows. All numeric scores were compared between PKU and control groups using the Mann-Whitney test while discrete characteristics, such as age, were compared using the Pearson Chi-Square test. The impact of PKU on several clinical outcomes, dental attendance, probability of being caries-free, and incidence of tooth wear, was examined through logistic regression.

### Results

#### Clinical Study

A total of 40 PKU children and 33 healthy controls were seen and examined during the six month study period. Table 1 describes the characteristics of the two groups, there being no significant difference in the age, sex, or numbers resident in areas with water fluoridation. There was little difference in the oral hygiene practices of the two groups, with all children brushing their teeth with fluoridated toothpaste either on their own or with the help of their mothers. Almost all the healthy control children (94%) and slightly less in the PKU group (90%) were reported to see a dentist at least once a year. Significantly more of the healthy control children (85%) and slightly less in the PKU group (79%) were reported to brush at least once a day.

### Table 1. A Summary of the Dental History of the Test and Control Children

<table>
<thead>
<tr>
<th>PKU (n = 40)</th>
<th>Male (46)</th>
<th>Female (43)</th>
<th>Mean age in years (+/-SD)</th>
<th>Fluoridated water (%)</th>
<th>Dental attendance (%)</th>
<th>Toothbrushing (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>23 (56)</td>
<td>17 (56)</td>
<td>8.76 (5)</td>
<td>37 (93)</td>
<td>14 (35)</td>
<td>16 (40)</td>
</tr>
<tr>
<td>Control (n = 33)</td>
<td>Male (56)</td>
<td>Female (56)</td>
<td>8.98 (3)</td>
<td>29 (88)</td>
<td>17 (50)</td>
<td>13 (40)</td>
</tr>
</tbody>
</table>

Table 2 describes the oral health indices of the two groups of children. There was no significant difference in the caries levels in either group of children, with 83% of the PKU and 79% of the control groups children being decay free. Interestingly, while there was no significant difference in the amount

#### Table 2. The Oral Health Indices of the PKU Compared With the Healthy Control Group of Children

<table>
<thead>
<tr>
<th>Caries free (%)</th>
<th>Mean plaque index (+/-SD)</th>
<th>Mean gingival inflammation (%)</th>
<th>Presence of tooth wear (%)</th>
<th>Wear typical of erosion</th>
</tr>
</thead>
<tbody>
<tr>
<td>PKU</td>
<td>33 (.83)</td>
<td>0.70 (.44)</td>
<td>0.54 (.1)</td>
<td>13 (.33)</td>
</tr>
<tr>
<td>Control</td>
<td>26 (.79)</td>
<td>.75 (.46)</td>
<td>.23 (.28)</td>
<td>8 (.24)</td>
</tr>
</tbody>
</table>

*Signifies statistical significance (P < 0.05).
of plaque and debris on the teeth of the two groups of children, those with PKU had significantly more gingival inflammation (P<0.05). A total of 33% (13) of the children with PKU had tooth wear. In four of the cases the type of wear, as indicated by the clinical appearance and affected sites, appeared to be mainly due to attrition. However, in the other nine there was distinctive occlusal "cupping" or "ditching" characteristic of erosion (Fig 1). In the control group, wear was seen in eight (24%) children, but in only two cases was it characteristic of erosion.

Discussion

The caries experience of the children with PKU in this study was generally low, with over 80% of children being caries-free. This is somewhat surprising given the potentially cariogenic nature of the PKU diet, in which protein is severely restricted and even the intake of fruit and vegetables must be calculated in the dietary prescription. The remainder of the recommended energy intake is provided by foods which are low in protein content but high in carbohydrate and fat. Daytime snacks may consist of small amounts of fruit, crisps, low protein biscuits, fruit sticks, sweet confectionery or sweetened beverages which are very low in phenylalanine. At times of intercurrent illness or poor growth, appetite is low and additional high energy snacks are encouraged. Young children may eat snacks as often as every two hours throughout the day; a diet, which might be expected to be associated with higher levels of caries. The lack of a significant increase in caries levels between children with PKU has been reported earlier.6-10 It has been suggested that phenylalanine may constitute a factor that limits the growth of plaque microorganisms and that this may explain the low caries rate in the presence of a highly cariogenic diet.11 Furthermore, in the current study there was no significant difference between the PKU children and the controls, both groups having significantly lower levels of caries than is reported for Australian children in general.15 The caries rates for this study are, in general lower than those reported earlier. This may reflect the change in pattern of use of fluoridated toothpastes and in their exposure to fluoridated water. Most (90%) of the children in the current study lived in areas supplied by optimally fluoridated water, a factor known to reduce the incidence of caries.16

Despite a slightly higher incidence of tooth wear among the PKU children compared with the controls, conclusions should be drawn with care. The dietary intake of the control children was not assessed, and yet it can be presumed that they, too, consume significant quantities of potentially erosive foods and drinks (i.e., citrus fruit, fruit juices, carbonated beverages, and sports drinks). In addition, defining the principal wear process occurring in any one mouth based upon the appearance of the teeth is somewhat subjective. Characteristic features of erosion are concave defects with smooth, rounded margins and a highly polished appearance. Attrition (tooth-on-tooth wear that may occur during grinding) results in a flatter wear facet limited predominantly to the incisal edges and molar cusps. Nevertheless, nine of the 13 PKU children who had signs of wear demonstrated features of erosion. Given the young age of the patients and hence the short time that the teeth may have been exposed to the acidic environment, these early signs are clinically significant.

While pH is considered to be important, the amount of titratable acid in a product is thought to give a more accurate indication of the erosive potential as it provides an

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**Table 3. Mean pH and Titratable Acidity of the Test Drinks and Controls**

<table>
<thead>
<tr>
<th>Drinks (n=5)</th>
<th>MD</th>
<th>MDF</th>
<th>MM</th>
<th>MDF</th>
<th>NXF</th>
<th>OJ</th>
<th>CC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean pH (+/- SD)</td>
<td>6.76 (0.01)</td>
<td>4.48 (0.01)</td>
<td>6.44 (0.01)</td>
<td>4.90 (0.02)</td>
<td>4.87 (0.02)</td>
<td>3.75 (0.02)</td>
<td>2.46 (0.01)</td>
</tr>
<tr>
<td>Titratable acidity in mEq/l (+/- SD)</td>
<td>4.18 (0.58)</td>
<td>126.80 (1.64)</td>
<td>14.40 (0.58)</td>
<td>92.86 (0.35)</td>
<td>86.80 (1.60)</td>
<td>109.50 (1.60)</td>
<td>38.56 (2.90)</td>
</tr>
</tbody>
</table>

(M D =XP M axamid, M DF =XP M axamid O range Flavoured, M M =XP M axamum, M MF =XP M axamum O range Flavoured and N XF =N ovamix Flavoured, O J =O range Juice, C C =Coca Cola) All results are statistically significantly different (P<0.05).
An important objective in health management is the prevention of disease initiation and progression. Identification of groups of children at risk of oral disease is important; children with PKU are, by the nature of their diet and dietary supplement, at risk of developing dental caries and tooth erosion. The management of these children and children with other inborn errors of intermediary metabolism has recently been reviewed.22 However, it is important for all health professionals involved in the care of these patients to be fully aware of these implications, to provide appropriate advice and to refer early for dental consultation. Good communication between the pediatrician, pediatric dentist and particularly a specialist dietician, is essential for effective management. Prevention in the form of appropriate use of fluoridated toothpastes and supplements, plus reducing the frequency of between meal snacks, will help to reduce the risk of dental disease. Furthermore, the consumption of water rather than soft drinks should be encouraged. However, it is important that any advice received by the patient/parent does not contradict advice received from other careworkers and that help is enlisted from both pediatricians and dietitians in reinforcing the need for daily preventive oral health measures in these children.

COnclusions

Based on the results of this study:

1. Children living in a water fluoridated area with phenylketonuria did not have significantly higher levels of dental caries than healthy controls. While the levels of plaque deposits were not significantly different, the children with PKU did exhibit more gingival inflammation.

2. Children with phenylketonuria did have a significantly higher incidence of tooth wear, of which erosive wear appeared to be the predominant process. However, the numbers involved in this study were small. Further study is required.

3. The amino acid supplements used in the management of children with phenylketonuria are potentially erosive with the flavored varieties in particular having a low pH and high titratable acidity.

4. There is a need for those responsible for the general care of children with phenylketonuria to be aware of the potential oral health problems.

References


PREVALENCE OF PRIMARY DENTITION CARIES IN HIV-INFECTED CHILDREN: A LONGITUDINAL STUDY.

B Carter, J Hicks, S Cron, C Flaitz, S Rossmann, C Simon, G Demmler, M Kline. Texas Children's Hospital, Baylor College of Medicine, University of Texas-Houston Health Science Center, Houston, TX.

The purpose of this longitudinal clinical study was to determine primary dentition caries prevalence in HIV-infected children, and to compare caries prevalence with CD4 percentage (CD4%) and immune suppression category. Forty-five children with vertical HIV transmission were evaluated for caries in the primary dentition at baseline and at 6 month intervals over a 24 month period. Caries prevalence was also compared with CD4% (>25%, 15-24%, <15%) and immune suppression category (immune suppression: none, moderate, severe). Caries in the primary dentition was expressed as dfs and dft. With primary dentition caries, comparisons were made among all children (2-9 yrs-old), and 2 to 4 yr-olds, and 5 to 9 yr-olds and compared with NHANES III data. Caries-free status was also determined.

Baseline Data

<table>
<thead>
<tr>
<th>Age</th>
<th>DFS (Mean)</th>
<th>DT (Mean)</th>
<th>Caries-free</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-9 yrs-olds</td>
<td>9.2</td>
<td>4.3</td>
<td>57%</td>
</tr>
<tr>
<td>2-4 yrs-olds</td>
<td>2.7</td>
<td>3.0</td>
<td>65%</td>
</tr>
<tr>
<td>5-9 yrs-olds</td>
<td>14.4</td>
<td>4.5</td>
<td>32%</td>
</tr>
</tbody>
</table>

Caries prevalence in HIV-infected children is considerably greater than in the US pediatric population, and increases with decreased CD4% and moderate to severe immune suppression. NIH-NIDR 1-RO1-DE11363