Are tablets a practical source of protein substitute in phenylketonuria?

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Background: A phenylalanine-free amino acid based protein substitute is necessary to provide the major source of protein in phenylketonuria (PKU). Protein substitutes in PKU are usually given as drinks. These are unpalatable and compliance is often poor. Tablets containing a suitable mixture of phenylalanine-free amino acids (Aminogran Food Supplement, UCB) are now available.

Aims: To compare the effectiveness and acceptability of these tablets with conventional protein substitute drinks.

Methods: Twenty one subjects with PKU, aged 8–25 years, participated in a randomised crossover study. During one phase, subjects received at least 40% of their protein substitute requirements from the amino acid tablets and the rest from their usual protein substitute tablets. During the other phase, they received their usual protein substitute. Each period lasted 12 weeks. Blood phenylalanine concentrations were measured at least once every two weeks and other plasma amino acids were measured at the beginning, at crossover, and at the end of the study. The subjects kept a diary of all protein substituent intake.

Results: Compliance appeared to be better with the new tablets than with patients’ usual protein substitutes. Ninety per cent (18/20) recorded that they took the tablets as prescribed, compared with 65% (13/20) fully compliant with their usual protein substitute. Moreover, plasma phenylalanine was lower on the amino acid tablets, and the median difference in blood concentrations between the two groups was 46 µmol/l (95% CI 14.8 to 89.0, p = 0.02). Tyrosine increased by a median of 16 µmol/l daily on the amino acid tablets (95% CI 7.1 to 40.5, p = 0.01). Most subjects (70%) preferred incorporating the new tablets into their usual protein substitute regimen.

Conclusions: Amino acid tablets are an effective and relatively popular protein substitute in older children, teenagers, and adults with PKU.
RESULTS

Nineteen subjects (13 female; six male) completed the study. One subject failed to start the study; one subject withdrew during the second treatment period as a result of the usual protein substitute appearing less acceptable after the phase on the amino acid tablets; and in a further subject the tyrosine concentration on the usual protein substitute was unavailable. Therefore, plasma phenylalanine data were available on 20 subjects on regimen B (amino acid tablets), and 19 subjects on regimen A (usual protein substitute). Plasma tyrosine data were available on 20 subjects on regimen B, and 18 subjects on regimen A. Ten subjects had regimen A first and 10 subjects regimen B first.

Dosage of protein substitute

On their usual supplement (regimen A), the median daily dose of prescribed amino acids was 66 g (range 32–75 g). On regimen B, nine (45%) of the subjects took their entire protein substitute as amino acid tablets. The other 11 subjects took between 40% and 65% of their protein substitute as tablets and the remainder as their usual protein substitute. The median daily dose of amino acid tablets was 42 (range 20–75), equivalent to 42 g amino acids. Overall, on regimen B, the median intake/day of amino acids in protein substitute was 60 g (range 48–75 g).

Effect on plasma phenylalanine concentrations

Plasma phenylalanine concentrations were significantly lower when subjects used the new amino acid tablets than when taking their usual protein substitute regimen (fig 1). The median plasma phenylalanine concentration on regimen A was 735 μmol/L, compared with 707 μmol/L on regimen B, but the median difference was 46 μmol/L (95% CI 14.8 to 89.0; p = 0.02). However, fig 1 also reveals a significant (p = 0.04) order effect in the crossover analysis. In the group receiving the new regimen B amino acid tablets first, the median A – B difference was 75 (95% CI 40.0 to 297; p = 0.01), whereas in the group receiving the usual regimen A first, the median difference was only 18 (95% CI –60 to 134).

Effect on plasma tyrosine concentrations

Plasma tyrosine concentrations showed a significant median increase of 16.0 when patients were taking the new tablets on regimen B (95% CI 7.1 to 40.5; p = 0.01; fig 2). Plasma tyrosine concentrations in patients on their usual protein substitute (regimen A) were not significantly changed, with a median rise of 1.8 (95% CI –14.5 to 25.8). There was no statistically significant evidence that the order of giving the regimen affected tyrosine change, as under regimen B there were median tyrosine increases of 12 and 40 given before or after regimen A respectively (p = 0.13).

Effect on other plasma amino acid concentrations

Plasma concentrations of the essential amino acids, other than phenylalanine, were almost all within normal ranges. The exceptions were isoleucine, leucine, threonine, and valine, which were each low in one patient on regimen A, and lysine, leucine, and threonine, which were each low in one patient on regimen B.

Acceptability of protein substitutes and compliance

Subjects considered that the tablets made their protein substitute regimen more acceptable (p < 0.05), according to results recorded by the visual analogue scale. On this scale, higher scores signified a more acceptable regimen. A mean of 57 (SD 35) was scored by patients on regimen A. Patients on regimen B, in which the tablets provided at least 40% of the protein substitute, scored a mean of 82 (SD 16). Overall, 70% of subjects preferred the amino acid tablets compared with the conventional protein substitute. Of these 14 subjects, six had the tablets first and eight had them second.
Compliance was better with the amino acid tablets. Thirteen subjects (65%) took the protein substitute as prescribed in regimen A, compared with 18 subjects (90%) for regimen B.

**Adverse events**

One subject had symptoms which appeared to be related to the Aminogran Food Supplement tablets. The symptoms were moderately severe diarrhoea and mild nausea, both of which started the day after taking the tablets. The diarrhoea continued for two weeks, and the nausea did not resolve while taking the tablets. Another adult subject had a significant weight gain while taking the tablets. Although the tablets were less effective in reducing plasma phenylalanine control, particularly when protein substitute powders to their usual protein substitutes. Despite the need to take a comprehensive vitamin and mineral supplements are available and compliance with separate vitamin and mineral supplements is poor.

This is the first full study to support the use of amino acid tablets in PKU. There has been one previous case report, describing a pregnant lady who packed her own capsules with amino acid powder and took 60 capsules daily. There is also one abstract describing two young adults who chose amino acid capsules in preference to other protein substitutes. In all three patients, blood phenylalanine control and plasma amino acids were satisfactory.

In summary, Aminogran food supplement tablets are an effective protein substitute for use in PKU. Most of the older children and young adults in this study preferred regimens incorporating these tablets to their existing protein substitute. Since compliance with protein substitute tends to be poor, it is particularly helpful to have an increase in the range of products from which patients can choose.

**ACKNOWLEDGEMENTS**

We thank the metabolic team at Dublin Children’s Hospital, who helped recruit some of the subjects to this trial, Mr Paul Davies, Institute of Child Health, Birmingham University; for all his help with the statistical analysis, and all the patients who took part.

**REFERENCES**

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Arch Dis Child 2003 88: 327-329
doi: 10.1136/adc.88.4.327

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