

Benefit of a prolonged release amino acid mix in PKU pregnancy

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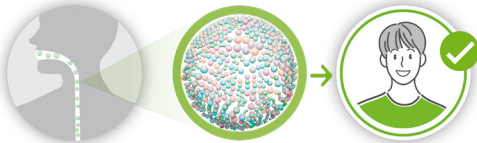
Summary

We present the case of a woman with PKU who, after the onset of pregnancy, was no longer able to follow the prescribed diet because the amino acid supplementation induced strong nausea and gastric reflux, with negative consequences on an optimal daily protein intake. The switch to an innovative prolonged-release amino acid preparation was a winning weapon: it was very well tolerated by the patient, who could successfully complete the pregnancy with the birth of a healthy child.

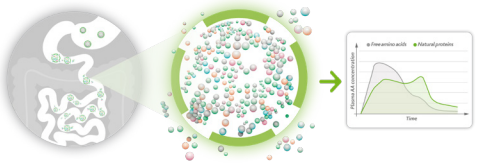
Background

- The impact of Phenylketonuria (PKU) is particularly critical during pregnancy, as elevated and prolonged intrauterine Phe levels have teratogenic effects to the developing fetus: this condition, known as 'maternal PKU syndrome', can cause various deficits including developmental delay, low birth weight, microcephaly, congenital heart disease, craniofacial dysmorphism, and intellectual disability¹.
- For this reason, women with PKU who are planning to have a child should follow a strict diet before conception and continue it throughout gestation, to keep Phe concentrations at safe levels (120–360 $\mu\text{mol/L}$) and prevent the complications of maternal PKU^{2,3}.
- It is crucial during pregnancy to replace natural proteins with amino acid mix that are often characterized by scarce palatability and frequently generate gastrointestinal discomfort, factors that contribute to poor dietary adherence and can make their intake particularly difficult during pregnancy⁴.
- Rigorous adherence to the strict PKU dietary regimen may be troublesome, especially if pregnancy-related symptoms such as nausea, vomiting, and gastrointestinal problems are present; this may prevent women from achieving proper metabolic control.
- A mixture of prolonged-release amino-acids with vitamins, minerals, and other nutrients performed very well in a pediatric PKU population⁵ and could be an effective option as a protein substitute for pregnant women with PKU. In particular, thanks to the formulation in small granules coated with functional additives, the content of the granules is gradually released in the small intestine, making the product tasteless and odorless, and allowing it to overcome practical problems associated with free amino acids, such as bitter taste, unpleasant smell, aftertaste and osmolality⁶.

Thanks to the special coating granules remain intact during consumption, masking amino acid odour and taste and preventing aftertaste. The result is a better palatability.



Granules begin to dissolve only at gut level and amino acid are gradually released. The result is a more physiological absorption in line with natural proteins with a protection from gastrointestinal discomforts.



Case presentation

We present the case of a young Italian woman (1985) with PKU who grew up without following any diet.

During childhood, she showed no particular problems apart from frequent abdominal pain, irritability, and a slightly impaired cognitive development. In adulthood, she led a normal life until she became pregnant: after some miscarriages, she was diagnosed with classic PKU at the age of 30 (blood Phe concentration = 1812.46 $\mu\text{mol/L}$ [29.94 mg/dl]).

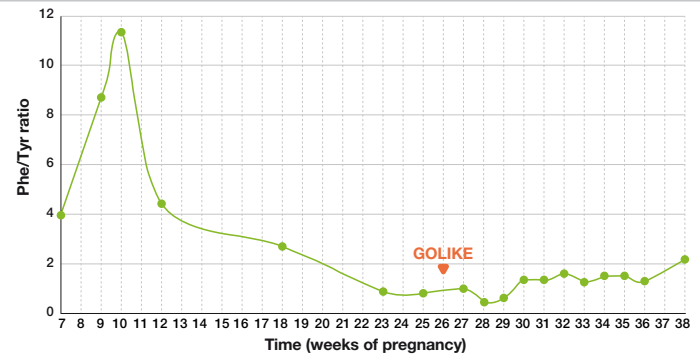
Subsequently, she started a strict dietary regimen with controlled Phe intake (697.28 mg daily) supplemented with two protein substitutes: 33 g daily of a slow-release large neutral amino acids (LNAA) preparation; a ready-to-drink product containing essential and non-essential amino acids, carbohydrate, vitamins, and minerals.

This diet allowed her to achieve optimal metabolic control, reducing her blood concentration of Phe to levels that did not interfere with a possible pregnancy. When she became pregnant again, her Phe values were within the safe range, and she was placed on a program for close monitoring of Phe levels (Figure 1).

CONCLUSIONS

The use of an innovative protein substitute with a prolonged-release formulation could be highly beneficial for pregnant women with PKU, allowing optimal metabolic control of Phe levels, contributing to prevent the complications of maternal PKU.

FIGURE 1: Phenylalanine/Tyrosine ratio over time. The red arrow indicates the start of Golike intake.

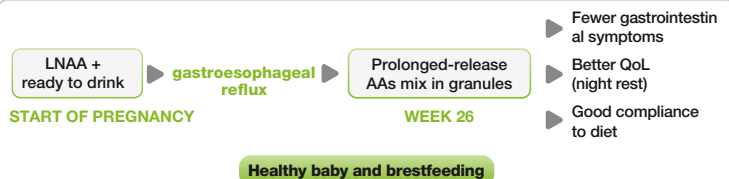


Unfortunately, the beginning of pregnancy coincided with the onset of a disabling gastroesophageal reflux, which prevented her from resting during the night.

This led to reduced dietary compliance and, consequently, worsened metabolic control. Thereafter, she was prescribed a new protein replacement, and from 26 weeks gestation she started taking (31.5g daily) a prolonged-release amino acid mixture with vitamins, minerals and other nutrients (PKU Golike 16+ APR Applied Pharma Research s.a). This product has been selected because many clinical studies evidenced safety of the excipients for use also during pregnancy and lactation^{7,8}.

The new supplement, administered with fruit juice, was very well tolerated by the patient, who reported a substantial reduction in gastrointestinal symptoms: the gastroesophageal reflux - which precluded night rest - disappeared, resulting in good compliance to the intake of the prescribed protein substitute, as indicated by the improvement of the phenylalanine/tyrosine (Phe/Tyr) ratio (Figure 1).

On the basis of this evidence, the dosage of prolonged-release amino acid mixture was doubled, to meet the protein-caloric intake of the third trimester of gestation.



The patient successfully carried to term her pregnancy with the spontaneous delivery of a healthy baby girl at 39 weeks. All auxological parameters of the newborn were within normal limits: birth weight = 2.73 kg; length = 48 cm; head circumference = 32 cm. After delivery, the mother continued to take the prolonged-release amino acid mixture with good adherence to dietary therapy and good metabolic control, which allowed her to breastfeed the child.

Discussion

The worsening of blood Phe control in PKU patients may cause a range of neuropsychiatric problems including depression, irritability, and reduced concentration ability. The situation is particularly delicate in the case of PKU women who plan to have a child: if they discontinued or liberalized their diet during adulthood, they most likely have Phe levels that are not safe for pregnancy and may encounter serious difficulties in returning to a strict dietary control and tolerating protein substitutes. Nutritional surrogates are often badly tolerated by PKU patients because of their bitter taste, smell, and aftertaste; moreover, they may cause gastrointestinal discomfort due to their osmolality^{5,9}.

This case is emblematic of how helpful an innovative prolonged-release protein substitute can be during gestation. Although the patient was highly motivated to follow the prescribed diet, given the failure of previous pregnancies, her tolerability to protein substitutes changed dramatically during the early stages of gestation due to gastroesophageal reflux, making it impossible to maintain a satisfactory metabolic control. Thankfully, switching to a prolonged-release amino acid supplement allowed the patient to obtain an optimal metabolic control. Furthermore, gastrointestinal pregnancy-related symptoms have been solved with an important improvement of patient's quality of life. Patient tolerated the protein substitute so well that she maintained the same dietary regimen after delivery, which gave her the opportunity to breastfeed the child.

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CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.