

given continuously for 3 years, whereas results following shorter treatment regimens were reported in most of the remaining studies (2). These factors may at least partly explain the extreme outcomes of the three influential studies, which were causing the heterogeneity of the original AR meta-analysis, and the lesson learned from this could be that characteristics of individual SIT products might also contribute to the different clinical outcomes.

Thus, excluding studies identified as extreme outliers from the AR meta-analysis (as generally advised within statistics) using influence statistics helped identify outliers and reasons for heterogeneity. Subsequently, the overall result of the AR meta-analysis was still clearly significant and without heterogeneity (Fig. 1C and D). However, there might be other cases where the outcome is less clear, and where very few patients can be pivotal for the final result.

In conclusion, caution should be exercised upon interpretation of results from meta-analyses with significant heterogeneity. We recommend including influence statistics and influence plots into the statistical guidelines of the Cochrane Library and in all meta-analyses impaired by significant heterogeneity.

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Fruit proteins: another cause of food protein-induced enterocolitis syndrome

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Key words: enterocolitis syndrome; fruit proteins.

A female patient presented recurring vomiting and hypotonia. The patient was full-term, initially breast-fed. At 2 months, a hypoallergenic formula was used to supplement breast-feeding because of positive fam-

ily history for atopy. At 4 months, solid foods (apple, pear and banana, crisps and tapioca) were introduced in her diet without any evident problem. At the 5th month of age, cow's milk (CM)-based formula (Humana plus[®]; Humana Italia S.p.A., Milan, Italy) was introduced. Patient developed repeated episodes of vomiting, hypotonia and diarrhoea few hours after the meal. CM allergy was diagnosed and a soy-based formula was substituted to supplement breast-feeding. Soy formula was continued for 15 days without troubles, suspended because of exclusive breast-feeding for 2 weeks, and then introduced again. At this time, soy supplementation was associated with frequent vomiting, hypotonia and lethargy. Similar reactions after reintroduction of apple, pear and banana occurred. She was admitted to local hospital and treated with intravenous fluid. A fructose challenge performed at 10 months of age in a local hospital was negative. An amino acid formula (Neocate[®]; SHS International Ltd, Liverpool, UK) was introduced; this was well tolerated and it was the only food used up to 12 months of age when she was admitted to our department for further evaluation.

At admission, the child's physical examination was normal; weight was 1 SD below the median. Evaluation included urine, stool cultures, toxicology and metabolic screening that resulted negative. Serum tests for specific IgE (Unicap; Phadia, Uppsala, Sweden) were negative except for CM (1.71 kUA/l). Skin prick tests (prick by prick) with pear, apple, banana, soy and CM resulted negative.

We performed an oral food challenge to CM, which resulted negative, and consequently, CM was added to her diet. An oral food challenge to soy was considered unnecessary, but soy was not allowed. Some days later, an oral food challenge with 10 g of mixed fruits (apple, pear and banana) was performed. The dose was administered gradually over a period of 45 min. Two hours later, the patient developed repetitive vomiting, had a decrease in blood pressure, and became lethargic. A complete blood count performed before challenge (2228/mm³ PMNs; 25.7% PMNs) was compared with the one performed 6 h after the challenge

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(11 961/mm³ PMNs; 67.2% PMNs) and it also indicated an increase of 5900 cells/mm³ in absolute neutrophil count after the challenge. Diarrhoea was observed the following day (tested haeme-positive). Gastric and esophageal biopsy revealed diffuse nonspecific inflammatory cell infiltrate with plasma cells and eosinophils.

She was treated with intravenous hydration and antihistamine, and was discharged home with the diagnosis of food protein-induced enterocolitis syndrome (FPIES) with the indication to avoid these and other fruits. The patient was well for a year when the accidental ingestion of peach juice was associated with the onset of the previous observed signs and symptoms.

In our patient, the challenge with mixed fruits fully satisfied the criteria for FPIES diagnosis (1). FPIES related to CM and soy is a well recognized entity. Additional causal foods such as egg, wheat, rice, oat, barley, string bean, pea, lentil, sweet potatoes, fish and poultry have been acknowledged as responsible (2–4), but fruit-induced FPIES has never been reported.

Frequently, patients with FPIES induced by foods other than CM or soy already have FPIES from CM or soy (2). The majority of the patients, as demonstrated in our case, usually loose milk sensitivity within 2 years from presentation (4).

The present study clearly shows that also proteins contained in fruits can be responsible of FPIES, which may have a prolonged course. Plant tissues contain thousands of different proteins (5) and it is difficult to identify the culprit antigens. Common related proteins such as nonspecific lipid transfer proteins, which are resistant to proteolysis and thermal treatment, and/or pathogenesis-related proteins might be the antigens responsible for the reaction.

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