Safety Benefits of an Increased Threshold in Milk-Allergic Patients: A Quantitative Risk Assessment Study

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Rationale

- The prevalence of IgE-mediated cow’s milk allergy in children is high, especially in younger age groups.
- This can be particularly concerning as cow’s milk protein (CMP) is a frequently detected unintended allergen in food products.
- Because of its ubiquitous distribution in foods and common consumption, it is particularly difficult to avoid cow’s milk.
- Accidental exposures can occur due to ingestion of food products that do not intentionally contain CMP but are contaminated with cow’s milk, or by accidental ingestion of food products that contain cow’s milk by recipe.
- Therefore, cow’s milk allergic (CMA) patients may be at a high risk of allergic reactions as a result of accidental exposure.
- Food immunotherapy can increase the eliciting dose (ED) threshold, which may reduce risk of reaction to CMP following unintended exposure.

Objective

- To assess the risk of experiencing an allergic reaction and to quantify safety benefits of increased ED thresholds in CMA patients by modeling the exposure to milk in 2 scenarios (accidental exposures and accidental ingestions) and comparing these with set ED thresholds in CMA patients.

Methods

Quantitative Risk Assessment (QRA)

- Consumption summary statistics for children aged 7–11 years from the 2007–2010 Dutch National Food Consumption Survey (DNFCS) and concentration of CMP in the consumed products were used to model exposures to milk protein in 5 food categories.
- A range of potential contamination levels based on literature surveys was used to create a set of ED thresholds.

Data Source

- Consumption estimate: mean 59.0 g (SD 29.6 ppm of CMP)
- Concentration of CMP in consumed products:
  - 1 mg of milk protein
  - 10 mg of milk protein
  - 30 mg of milk protein

Results

Accidental Exposure Scenarios

- Percentage of eating occasions predicted to result in allergic reaction for accidental exposure to non-packaged bakery items contaminated with cow’s milk (Figure 2) were used to calculate relative risk reductions.
- For non-packaged bakery products, a relative risk reduction of at least 82.3% was achieved when the ED threshold was increased from ≤30 mg to 300 mg, and up to 99.8% when increased to 1,000 mg (Figure 2).
- Similar results were seen for the other food categories:
  - 74.2% to 99.7% when the ED threshold was increased from ≤30 mg to 300 mg, and 96.9% to 99.8% when the ED threshold was increased to 1,000 mg.

Accidental Ingestion Scenarios

- For products that contained cow’s milk as an ingredient, relative risk reductions were lower but still clinically relevant compared with accidental exposures.
- For non-packaged bakery products, a relative risk reduction of at least 51.6% was achieved when the ED threshold was increased from ≤30 mg to 1,000 mg (Figure 3).
- The relative risk reductions were similar for other food categories: 48.8% to 99.2% when the ED threshold was increased from ≤30 mg to 1,000 mg, and 47.8% to 99.9% when the ED threshold was increased to 1,000 mg.

Conclusions

- In CMA children, accidental exposure or ingestion of products containing cow’s milk can pose substantial risk for experiencing an allergic reaction.
- Increasing a milk-allergic patient’s ED threshold to 300 mg or 1,000 mg of CMP resulted in a clinically relevant reduction of modeled risk for a reaction to cow’s milk–contaminated food products.
- For food products that contain dairy as an intended ingredient, the modeled risk reduction for an allergic reaction upon accidental ingestion by increasing the ED threshold to 300 or 1,000 mg of CMP was less pronounced, yet still potentially clinically meaningful.