

Milk allergy tapered to dahi culture

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Introduction:

Casein and whey proteins in mammalian milk are often the first major allergens infants encounter.¹⁻² Cow's milk protein allergy (CMPA) is subsequently among the most common diagnoses in infants, with a prevalence of 2 to 3% in the first years of life.²⁻³ Oral food challenges (OFCs) have provided evidence of reduced allergenicity from food processing.⁵ Heat-labile allergens are denatured during extensive thermal processing, enabling baked milk tolerance among some patients with CMPA.⁵⁻⁷ We describe a pediatric patient with history of CMPA who safely passed a baked-milk OFC and tolerated the traditional South Asian fermented milk dahi, which has only previously been tested in mouse models.⁸

Case description:

A 4-year-old male of South Asian descent with history of CMPA presented with his mother for allergy evaluation. He had been medically advised to avoid all dairy. His mother recalled an accidental dairy encounter at 2 years old when he had quickly demonstrated gastrointestinal irritability and ocular erythema, pruritus, and epiphora. On different occasions, he reacted to ice cream and Alfredo sauce with ocular erythema, throat discomfort, and dyspnea, treated with diphenhydramine.

A diagnosis of CMPA was based on a positive skin-prick testing (SPT) to milk (11-mm). The patient later tolerated the traditional baked-milk OFC in a controlled setting. On subsequent challenge, he was able to tolerate his mother's homemade yogurt dahi, as long as it was fermented for at least 10 hours before consumption. His parents reported failure of commercial dairy yogurts in the past. He continued

regular consumption of his mother's homemade dahi.

Discussion:

IgE-associated symptoms appear immediately or within two hours after CM ingestion and affect integumentary [angioedema, urticaria, atopic dermatitis (AD) exacerbation], respiratory (wheezing or stridor, dyspnea), and/or gastrointestinal systems (vomiting), complicating to systemic anaphylactic reactions (bronchoconstriction, tachypnea, dysphagia, facial flushing or pallor, hives, pruritis) in severe cases.^{1,3} Thorough medical history and physical examination considering these symptoms is the first step in appropriate diagnostic procedures.³

Sensitization to CMP and, hence, an ongoing IgE-mediated immunological process, is indicated by the presence of cow's milk-specific serum immunoglobulin E (sIgE, ≥ 15 , >95% PPV) and/or positive skin prick testing (SPT; ≥ 8 , >95% PPV).³ The degree of antibody titers and SPT reaction diameter are useful clinical indicators of CMPA persistence and CMP reaction probability.³ Further diagnostic work-up for specific sIgE reactivity to CMP casein (80%; α S1-casein, α S2-casein, β -casein κ -casein) and whey (20%; bos d 4-7) fractions is often not clinically indicated due to poor specificity, since 75% of patients are reactive to at least several different proteins.¹ These laboratory evaluations, in the context of a thorough history and physical examination, are confirmed by a diagnostic allergen elimination test, even in cases of negative specific sIgE results.³

A successful allergen elimination diet of 1 to 2 weeks demonstrates improvement of the clinical symptoms.³ This is succeeded by the final confirmatory or exclusionary step, a standardized oral food challenge (OFC) under medical supervision.³ Regardless of the individualized diagnostic approach and plan, optimal management of food allergy involves monitoring appropriate growth and nutrition, accidental ingestions or exposures, potential for food allergy resolution and/or new developments, and psychosocial impacts of food allergy; prescribing emergency medications as indicated for anaphylactic episodes; and offering anticipatory guidance and family education on living with food allergies.³

Re-evaluating potential for resolved food allergies with OFCs is often involved in the continued plan of care.³ Patients with CMPA and no history of severe anaphylaxis to CMP may tolerate an OFC with baked-milk products (e.g., muffins, cakes), which induces conformational protein modification and, hence, may reduce allergenicity.³ Conformational epitopes, which are food polypeptides folded in three-dimensional structures, are subject to chemical changes, unfolding, and/or aggregation that reveal new epitopes and denature previously recognized patterns for IgE-binding.⁴ Secondary milk processing techniques, such as pasteurized, boiled, powdered, and hydrolyzed, have demonstrated reduced IgE reactivity but incomplete abolishment of CMP structure and, subsequently, allergenic activity.⁴

Other potential milk processing that minimized allergenicity, enabling consumption, lacks sufficient clinical evidence.⁴ Fermentation has recently been proposed as an alternative processing technique to enable tolerable milk consumption for patients with CMPA.⁴ Lactic acid fermentation provides a reduced pH that hydrolyzes and aggregates proteins.⁴ Reduced allergenicity through fermentation is more strongly evidenced in soybeans,⁴ as most milk fermentation processes have only been studied at the molecular level.⁸ Heat-treated lactic acid bacteria (LAB) strain R-037 (*Lactobacillus delbrueckii* subspecies *lactis*) isolated from the traditional South Asian fermented milk dahi in Watanabe *et al.* suppressed elevated sIgE and AD inflammatory auricular thickness in mouse models (ovalbumin-induced type 1 allergy and NC/Nga

model mice).⁸ Watanabe *et al.* and the present case emphasize the role of specific starter culture bacterial strains and/or pH involved in thermal processing, fermentation, and cooled storage as key determinants of proteolytic degradation and consequential bioactivity of milk peptide allergens.⁸

The active cultures in dahi are similar to all commercial brand yogurts but are subject to a specific, traditional fermentation method: (1) boiling until 15-20% volume reduction; (2) cooled to body temperature; (3) inoculated with 2-3% starter (i.e. previously made dahi); (4) stored in earthenware vessel, wrapped with a woolen cloth, straw, or jute bag; (5) kept overnight for at least 10 hours to induce curd formation.⁸

Conclusion:

The present case is the first human report of a successful oral food challenge to traditional South Asian fermented milk dahi. Diverse temperature combinations, reactivity with water or other ingredients, levels of processing, and diagnostic measures have cautioned further exploration of alternative milk preparations that are safe for consumption in those with history of cow milk protein allergies. Further research is indicated to further analyze the make-up and allergenicity of the resultant proteins/peptides from different milk processing methods.

Author Contributions:

All authors contributed equally to the conception and design, acquisition of data, or analysis, interpretation of data, manuscript preparation and review.

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Potential Conflicts of Interest Disclosures:

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