Peer Review Article

# THE ROLE OF FOOD ALLERGY IN RHINITIS AND NASAL POLYPOSIS

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## ABSTRACT

Many patients feel that their rhinitis is triggered by foods. Although patients with rhinitis are frequently sensitised to foods, there is little evidence to support the role of food allergy in causing rhinitis in isolation. The presence of food allergy in infants may be a marker for subsequent development of allergic rhinitis. While many patients associate the ingestion of cow's milk with an increase in the production and thickness of nasal secretions, milk and dairy product intake has not been found to be associated with an increase in symptomatic congestion or an increase in nasal secretions. Respiratory symptoms alone, as a manifestation of cow's milk allergy, are rare. Food additive intolerance may manifest as chronic rhinitis. Tartrazine sensitivity may be present in aspirin-sensitive patients due to the similarity in the molecular structure of tartrazine to aspirin. The prevalence of sensitisation to foods is higher in patients with chronic sinusitis with nasal polyps than controls but there are no reported studies on the efficacy or effects of dietary restrictions on chronic rhinosinusitis.

## FOOD ALLERGY

Food allergy is an immune-mediated non-toxic reaction to food, which may be IgE-mediated or non IgE-mediated.[1] Oral ingestion is the primary route of exposure to food allergens, but the symptoms may rarely occur from direct inhalation of aerosolised particles containing allergenic food. Sixteen percent of patients in an Australian cohort of children with seafood allergy experienced rhinorrhoea and nasal pruritus on exposure to seafood vapours.[2]

### EPIDEMIOLOGY OF FOOD ALLERGY

Both the prevalence and spectrum of food allergens differ considerably between geographical regions.[2] Food allergy is most prevalent in the first two years of life, with the prevalence at one year of age estimated at 6-8 percent, falling to about 1-2 percent in late childhood and remaining stable thereafter through to adulthood.[3] The point prevalence of self-reported food allergy is approximately six times higher than that of challenge-proven food allergy.[4]

The most common food allergies in young children are cow's milk (2.5%), hen's egg (1.3%), peanut (0.8%), wheat (0.4%), soya (0.4%), tree nuts (0.2%), fish (0.1%), and shellfish (0.1%).[3] Half of the infants who have an IgE-mediated cow's milk allergy develop sensitivity to other foods. Allergies to milk, soy, eggs, and wheat are likely to resolve in adulthood but other food allergies are more likely to persist. Adults are frequently allergic to shellfish (2%), peanuts (0.6%), tree nuts (0.5%), and fish (0.4%).

It is difficult to identify the true prevalence of food-induced allergic rhinitis, because it frequently occurs in association with other food allergy symptoms such as asthma, eczema, oral allergic manifestations, urticaria, and gastrointestinal symptoms.

## RHINITIS

### DEVELOPMENT OF RHINITIS IN PATIENTS WITH FOOD ALLERGY

The presence of food allergy in children has been associated with the subsequent development of respiratory allergy, as part of the atopic march.[5] In the Isle of Wight study, the presence of egg allergy was associated with the development of respiratory allergy, with a positive predictive value of 55%,[6] while the German Multicenter Allergy Study found the presence of hen's egg allergy at the age of 12 months to be a marker for sensitisation to indoor and outdoor inhalant allergens at 3 years.[7]

Huang et al. studied a cohort of patients with rhinitis due to milk allergy proven on oral food challenge.[8] Although the prevalence of cow's milk allergy decreased from 100%

to 0% by the age of 5 years, there was an increase in the prevalence of respiratory allergy from 0% to 72.2% at 5 years. There was a similar decrease in the prevalence of egg allergy from 100% to 11.1% with the prevalence of respiratory allergy in these patients increasing from 0% to 44.4%.

## PATIENTS' OPINIONS

Patients often feel that foods trigger their rhinitis symptoms. In a survey of patients with allergic rhinitis in primary health care in South Africa, 29.1% of patients felt that foods triggered their allergic rhinitis either moderately (16.2%), quite a lot (6.9%) or a great deal (6.0%).[9] Patients at the paediatric allergy clinic in Bloemfontein felt that their allergic rhinitis was triggered by dairy products in 8% of cases, food additives in 5% and other foods in 3.5%.[10]

## SENSITISATION TO FOODS

Patients with rhinitis are frequently sensitised to foods. In a large population-based sample of schoolchildren aged 9-11 years in France, asthma and allergic rhinitis were found significantly more frequently in children with food sensitisation, those with reported symptoms of food allergy and children with skin prick-tested (SPT) food allergy, than children without.[11] Mercer et al. reported sensitisation to fish (sIgE 5.9%, SPT 26.2%), milk (sIgE 9.9%, SPT 30.6%) and wheat (sIgE 24.4%, SPT 30.6%) in children with allergic rhinitis.[10] In a study of 123 patients with rhinitis aged 4-78 years, Corey et al. found sensitisation to foods in 25 (20.3%) of patients, with the most common sensitising foods being peanut in 16 patients, milk in 14 patients and corn in 13 patients.[12] In adult patients with allergic rhinitis, Sahin-Yilmaz et al. found sensitisation to peanut in 23.4%, shrimp in 22.2% and milk in 13.2%.[13]

Gendeh et al. conducted a prospective matched, controlled study of 148 patients adult patients with rhinitis in Kuala Lampur.[14] Patients with rhinitis had a significantly higher rate of positive SPT for foods than controls (47.9% vs. 4.4%). Foods with positive SPT in the rhinitis group were shrimp (47.9%), rice (30.4%), crab (24.3%), cheese (14.5%), beef (12.2%), milk (11.5%), chocolate (11.5%), mussel (11.5%), banana (6.3%), wheat (4.7%), and egg (3.3%). House dust mite sensitisation was also significantly more common in the rhinitis group (72.3%) than the control group (22.5%). The authors felt that the high incidence of food allergy could be partially due to cross-reactivity between foods and aeroallergens, particularly tropomyosin in shrimp and house dust mites. Gastrointestinal symptoms (bloating, flatulence, nausea, and abdominal pain) were significantly more common in rhinitis patients than controls, but the authors did not provide any evidence that these symptoms were as a result of food allergy.

## CHALLENGE TESTING

Nasal symptoms accounted for 70% of the respiratory symptoms in children who underwent double-blind, placebo-controlled food challenges (DBPCFC) but rarely occurred in isolation.[15] Kumar et al. evaluated 1860 patients with asthma and/or allergic rhinitis, 1528 of whom had allergic rhinitis, for the presence of food allergy.[16] Of these patients, 1097 (58.9%) gave a history of food allergy, with allergies being reported to curd (48.1%), rice (43.9%), citrus fruits (35.2%), banana (27%), milk (11.9%) and blackgram (9.7%). The most common positive SPTs were rice (6.2%), blackgram (5.9%), lentil (5.5%), citrus fruits (5.3%), pea (3.8%), maize (3.8%) and banana (3.6%). Although 21 (46.6%) of the 45 patients who underwent DBPCFC had positive reactions, nasal symptoms only occurred in 2 patients.

## HYPOALLERGENIC DIET

Ogle and Bullock reported on 322 children with allergic rhinitis (320 patients) and/or asthma (273 patients).[17] Eighteen (6%) of these children also had atopic dermatitis and 22 (7%) had gastroenteropathy. When placed on a hypoallergenic diet consisting of Meat Base Formula, beef, carrots, broccoli and apricots, 91% of patients improved. Symptoms were reproduced in 51% of children on challenge testing, with patients responding to milk (29%), egg (7%), chocolate (5%), soy formula (5%), legumes (4%), corn (4%), rice (2%), citrus (2%) and apple (2%). Forty percent of children later developed an inhalant allergy. Only 6% of children followed up for at least 5 years continued to have food sensitivity.

## COW'S MILK ALLERGY

Patients often associate dairy products with an increase in nasal secretions. While rhinitis occurs in 10-30% of children with cow's milk allergy, respiratory symptoms alone, as a manifestation of cow's milk allergy, are rare.[8] Pinnock et al. investigated the relationship between milk intake and mucus production in young adults and found that milk and dairy product intake was not associated with an increase in symptomatic congestion or an increase in nasal secretions.[18]

## FOOD ADDITIVES

It is estimated that 6-8% of patients classified as having non-allergic perennial rhinitis have additive intolerance.[19,20] The food additives sodium benzoate, butylated hydroxyanisole, sodium metabisulfite and monosodium glutamate have been reported to cause chronic rhinitis as determined by elimination diets and double blind placebo controlled oral challenge[20-23] while a case of polyposis due to sodium glutamate intolerance has also been reported.[24]

Rhinitis appears within 6 hours of a single provoking dose of the offending additive and symptoms last for at least 2 days.[19] The pathogenic mechanism of additive-induced rhinitis remains unclear but is believed to be non-immunologic, as skin prick tests and patch tests with the offending food additives produce negative results.[19] Histamine is believed to play a part in the pathogenesis

as antihistamines are effective in controlling symptoms in most patients.[19]

## NASAL POLYPS

Samter's triad is the triad of nasal polyps, asthma and aspirin intolerance.[25] Aspirin sensitive patients may have respiratory symptoms (rhinitis and/or asthma) or urticaria or both on ingestion of aspirin.[25,26] In their description of the triad, Samter and Beers also described food sensitivity in 14.3% of patients, which they attributed to sodium benzoate and tartrazine in most cases.[25] Tartrazine sensitivity is reported to be present in 8-50% of aspirin-sensitive patients and is believed to be due to the similarity of the molecular structure of tartrazine to aspirin.[25-28] Although a double-blind placebo controlled cross-over challenge in atopic adults found that tartrazine was no more likely than placebo to cause adverse reaction in patients with allergic rhinitis, asthma, urticaria or pseudo-allergic reactions to non-steroidal anti-inflammatory drugs, this was a small study in which only five of the 26 patients were sensitive to either ASA or NSAIDS.[29] Diets avoiding high-salicylate foods may reduce exacerbations but are difficult to follow.[30]

In a postal survey of 900 patients with nasal polyps, 5.9% reported that they had a known food allergy.[31] In a prospective study of 80 patients with nasal polyps, 81% of patients had positive intradermal tests for food allergens as compared to 11% of controls, with the most common reactions being to wheat, potato, and tomato.[31] In a follow up study, 70% of patients with nasal polyps were found to have positive intradermal food tests (IDFTs) vs 7% of controls, while there was no significant difference in the prevalence of positive SPT to aeroallergens in nasal polyp patients (43%) as compared to controls (48%).[32] The authors therefore felt that the IDFT positivity reflected a specific response to food rather than being a simple marker of atopic status.[32] However, IDFTs have a low specificity and are not recommended for food allergy testing.[4,33] The authors did not provide any evidence for a causal role of food allergy in the pathogenesis of the nasal polyps.

In a group of patients with chronic sinusitis with nasal polyps, significantly more patients (14%) were sensitised to milk compared with none of the tested healthy controls while there was no difference in sensitisation to wheat,[34] but once again there was no evidence provided of causality. While some patients adopt dairy-free diets with subjective benefit, there is no objective proof of any benefit.[30] There have not been any double-blind, placebo-controlled studies that have tested the efficacy or effects of diet on chronic rhinosinusitis.[30]

## CONCLUSION

The presence of food allergy in infants may be a marker for the subsequent development of allergic rhinitis. While sensitisation to foods is often present in patients with allergic rhinitis, there is little evidence to support the role of food allergy in causing rhinitis. Food additive intolerance may play a role in causing rhinitis while tartrazine may exacerbate symptoms in aspirin sensitive patients. Sensitisation to foods may be present in patient with nasal polyposis but there is no evidence to support dietary modification in these patients.

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### For asthma

The long-term goals of asthma management are to achieve good control of asthma symptoms in order to maintain normal activity levels as well as to minimise future risk of exacerbations, fixed airflow limitation and side effects.[1] At each treatment step in asthma management, AstraZeneca has several different medication options available, classified as 'preferred' medication by GINA guidelines[1]:

- Step 1 treatment is with an as-needed short-acting beta-2-agonist (SABA) alone such as Bricanyl® Turbuhaler®.
- Step 2 treatment is a regular daily low-dose inhaled corticosteroid (ICS) such as Pulmicort® Turbuhaler® + SABA as needed.
- Step 3 treatment for persistent symptoms and/or exacerbations despite low-dose ICS is a combination ICS/long-acting beta-2-agonist (LABA) such as the fixed-combination dry powder inhaler (Symbicord® 80(160)/4,5 Turbuhaler®), the fixed-combination metered dose inhaler Vannair® 80(160)/4,5 Inhaler or the use of separate inhalers i.e. Pulmicort® Turbuhaler® together with the LABA in Oxis® Turbuhaler®. The use of low-dose budesonide/formoterol as both maintenance and reliever therapy, such as Symbicord® SMART, has been shown to reduce the risk of exacerbations, compared with maintenance controller treatment plus as-needed SABA.
- Step 4 treatment is with medium- or high-dose ICS together with a LABA such as Symbicord® 320/9 Turbuhaler® or Vannair® 160/4,5 inhaler.

### For COPD

Appropriate pharmacologic therapy can reduce chronic obstructive pulmonary disease (COPD) symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance.[2] Each treatment regimen needs to be patient-specific as the relationship between tolerance of symptoms, airflow limitation and severity of exacerbations will differ between patients.[2] The choice between beta-2-agonist, anticholinergic, theophylline or combination therapy depends on availability and individual patient response.[2]

- Bronchodilator medicines are given either on an as-needed basis with a SABA such as Bricanyl® Turbuhaler® or on a regular basis with a LABA such as Oxis® Turbuhaler® to prevent or reduce symptoms.[2] LABAs are more convenient for patients and more effective at producing maintained symptom relief than SABAs.[2]
- An ICS/LABA combination such as Symbicord® Turbuhaler® or Vannair® Inhaler is more effective than the individual components in improving lung function and health status and reducing exacerbations in patients with moderate to severe COPD.[2]

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S4 Vannair® 80:4,5 (Inhaler). Reg. No: A39/21.5.1/0506. S4 Vannair® 160:4,5 (Inhaler). Reg. No: A39/21.5.1/0507. Each single actuation contains as active constituents, Budesonide 80 or 160 µg and formoterol fumarate dihydrate 4,5 µg. PHARMACOLOGICAL CLASSIFICATION: A 21.5.1 Corticosteroids and analogues. INDICATIONS: Asthma: VANNAIR® 80:4,5 & 160:4,5 µg/dose is indicated in the treatment of asthma in adults and children 6 years and older where continued use of a combination (inhaled corticosteroid and long-acting beta-2-agonist) is appropriate. COPD: VANNAIR® 160:4,5 µg/dose is indicated in the regular treatment of patients with moderate to severe chronic obstructive pulmonary disease (COPD), with frequent symptoms and a history of exacerbations. For full prescribing information refer to the package insert approved by the medicines regulatory authority.

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S4 Oxis® Turbuhaler® 9 (Inhaler). Reg. No: 32/10.2.1/0168. Each dose delivers: formoterol fumarate dihydrate 9 µg. The corresponding metered dose contains 12 µg formoterol fumarate dihydrate. PHARMACOLOGICAL CLASSIFICATION: A 10.2.1. Bronchodilators (inhalants). INDICATIONS: Add on therapy to maintenance treatment with inhaled corticosteroids for the prophylaxis and treatment of reversible airways obstruction in asthma, chronic bronchitis and emphysema and prevention of bronchospasm in exercise-induced asthma, when adequate treatment with corticosteroids is not sufficient. For full prescribing information refer to the package insert approved by the medicines regulatory authority.

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