

Effects of omalizumab in patients with food allergy

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ABSTRACT

Omalizumab is a novel therapy approved for treating patients with moderate to severe persistent allergic asthma with a serum IgE ranging from 30 to 700 IU/mL. We examined the efficacy of omalizumab as a treatment for IgE-mediated food allergy. An Institutional Review Board–approved prospective pilot study was performed to assess the efficacy of omalizumab in 22 patients with persistent asthma and concomitant IgE-mediated food allergy. All patients showed skin test positivity to foods and experienced allergic food reactions based on history. Patients were interviewed on unintentional and/or unauthorized exposures to sensitized foods. Thirteen female and nine male patients (range, 4–66 years old; mean, 38 years) were evaluated in a private practice setting. Mean IgE level was 1120.74 IU/mL. Sensitized allergens included fish, shellfish, peanuts, tree nuts, egg, soybean, and wheat. All 22 (100%) patients maintained significant improvement as shown by a decrease/lack of clinical symptoms on reexposure to sensitized foods. Clinical improvement by the sixth dosage of omalizumab (150–300 mg q. 2–4 weeks) was noted by history and physical examination. Eight patients noted a decrease in their food-induced atopic dermatitis, 13 patients noted a decrease in their food-induced asthma symptoms, 3 patients noted a decrease in their food-induced urticaria, 6 patients noted a decrease in their food-induced rhinosinusitis symptoms, and 9 patients showed efficacy for angioedema and/or anaphylaxis. While treating asthma patients with omalizumab, patients subjectively observed a reduction in their concomitant IgE-mediated food allergy symptoms.

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Approximately 3–4% of adults in the United States have food allergies¹ and the incidence is likely increasing. Food allergies are the most common cause of anaphylaxis and no pharmacologic treatments are available to prevent a reaction. The emergency use of epinephrine, antihistamines, and steroids are usually successful in treating a systemic reaction that is already underway. The only true treatment to prevent a reaction is strict avoidance of the offending food with careful monitoring of all consumed food. Reading food labels can be confusing because many packaged goods do not name the allergic food such as peanuts in the ingredient list but report on their labeling, “may contain peanuts/nuts,” or “processed in a facility that also processes peanuts/nuts.” Peanut protein has been found in up to 10% of packaged goods with this advisory labeling.²

Strict avoidance of allergic food is particularly difficult in children who often are too young to understand food allergy and also unable to monitor their food consumption. Children also have an increased prevalence of food allergies compared with adults. Children often outgrow their food allergies including cow’s milk and egg allergies; however, allergy to shellfish and peanuts/tree nuts are usually not outgrown. Peanuts/tree nuts are the allergens causing the majority of food-induced fatal anaphylaxis in young adults.³ Accidental food exposure to the offending allergen is common, unpredictable, and, on rare occasion, can be fatal.

Omalizumab (Xolair; Genentech, South San Francisco, CA) is a recombinant humanized monoclonal antibody to IgE. It is usually prescribed in the treatment of adults and adolescents ≥ 12 years old with moderate to severe persistent allergic asthma with elevated IgE, ranging from 30 to 700 IU/mL. Omalizumab prevents the type 1, immediate hypersensitivity, allergic reaction by binding IgE in the serum and preventing its binding to the high-affinity Fc ϵ RI. It has been shown to be effective for asthma,⁴ allergic rhinitis,⁵ and, in case reports for chronic rhinosinusitis,⁶ chronic urticaria,⁷ angioedema,^{8,9} and atopic dermatitis.¹⁰ Considering omalizumab’s efficacy in these IgE-mediated diseases, it may have a therapeutic role in IgE-mediated food allergies.

The objective of this study was to examine patients being treated with omalizumab for asthma who also

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Table 1 Food allergy patients and changes with Xolair

Patient Initials	Sex	Age (yr)	Pretreatment Serum IgE Level (kU/L)	Xolair Dose	Skin Test Sensitivity	Allergic Reaction	Efficacy of Omalizumab on Food Allergy
IA	M	43	3288	300 mg q. 2 wk	Clam, tuna, crab, lobster, shrimp, wheat; salmon, scallops, blackberry, and blueberry	Crab/lobster/shrimp caused hives and exacerbation of atopic dermatitis	After dose 10, patient was able to eat shrimp and lobster without hives or atopic dermatitis exacerbation
CB	F	46	4237	300 mg q. 2 wk	Lobster, perch, smelt, salmon, shrimp, cashew, pecan, pistachio, and almonds	Lobster, crab, shrimp, nuts anaphylaxis, hives, swelling, and wheezing	After dose 3, patient ate peanuts and only has mild rash on face; after 11th dose, ate avocado and only had hives and wheezing; after dose 14, ate assorted nuts without anaphylaxis; after 19th dose, ate almonds without problems
MB	F	48	1918	300 mg q. 2 wk	Anchovy, apricot, pepper, poppy seed, peanut, pecan, tuna (4+), shrimp, lobster, scallops, cantaloupe, blueberry, lemon, and grape	Food allergies are associated with atopic dermatitis and asthma exacerbations.	Asthma and atopic dermatitis improved significantly after dose 3; patient was able to eat fish without asthma nor atopic dermatitis relapse
SB	F	33	343	150 mg q. 2 wk	Seafood mix, egg white, and soy	Shellfish anaphylaxis	After dose 1, tolerated shellfish after cooking for 30 min; after 5th dose, able to eat shrimp without anaphylaxis (only scratchy throat)
CB	M	14	599	300 mg q. 2 wk	Wheat and tree nut allergy	Atopic dermatitis, chronic sinusitis, GERD and gastritis, and hives	After dose 6, patient was able to consume wheat without relapse of asthma, atopic dermatitis, and CRS

Table 1 Food allergy patients and changes with Xolair (Continued)

Patient Initials	Sex	Age (yr)	Pretreatment Serum IgE Level (kU/L)	Xolair Dose	Skin Test Sensitivity	Allergic Reaction	Efficacy of Omalizumab on Food Allergy
MB	F	51	46.6	150 mg q. 4 wk	Parsley, hazelnut, rye, wheat, peanut, cucumber, endive, rice milk, pecan, rice, pepper; cantaloupe, cranberry, strawberry, avocado, broccoli, olive, string bean, and watermelon	Chronic sinusitis, migraine HA, allergic rhinitis, and asthma	After dose 1, migraine HA improved despite wheat consumption; after dosage 5, CRS, asthma, and migraine HA improved despite eating peanuts and/or berries
JC	M	16	1818	300 mg q. 2 wk	Brazil nut, cashew, peanut asparagus, cabbage, tomato, buckwheat, corn, rice, lima bean, soybean, and cow's milk	GI symptoms—nausea, stomach aches, sweating, and erythema of extremities; atopic dermatitis	After dose 7, patient can tolerate pizza, chocolate chip cookies without GI symptoms; he also tolerates wheat and most allergic foods after the 9th dosage
HC	F	33	355	300 mg q. 2 wk	Shellfish, soybean, corn, peanut, green pea, and edamame	Asthma, AD, CRS, and GERD all improved on Xolair with rechallenge	After dose 4, patient is able to eat corn, soybean, and green peas without exacerbations of asthma, CRS, AD, and GERD
RC	M	13	2600	150 mg q. 2 wk	Corn, seafood mix (shrimp, crab, lobster, codfish, tuna, and salmon); tree nut mix, peanut, egg white, soy, cashew, hazelnut, peanut, pistachio, and walnut	Angioedema, asthma, and anaphylaxis	After dose 1, ate shrimp without asthma or systemic reaction (prior anaphylaxis)
PD	M	57	99.5	150 mg q. 2 wk	Shrimp and cow's milk	Chronic sinusitis, GERD / gastritis, migraine HA, and asthma	After dose 5, patient able to tolerate cow's milk without chronic sinusitis, asthma, or HA symptoms

Table 1 Food allergy patients and changes with Xolair (Continued)

Patient Initials	Sex	Age (yr)	Pretreatment Serum IgE Level (kU/L)	Xolair Dose	Skin Test Sensitivity	Allergic Reaction	Efficacy of Omalizumab on Food Allergy
SE	M	47	281	150 mg q. 2 wk	Cow's milk, seafood mix, soy, wheat/rye, crab, peanut, corn, and salmon	Atopic dermatitis and severe urticaria	After dose 4, severe urticaria resolved despite never eliminating sensitized foods
ME	F	43	1538	150 mg q. 2 wk	Seafood mix, tree nut mix, peanut, wheat/rye, lobster, codfish, figs, coconut, almond; cow's milk, egg white, and soy corn	Wheat/corn/cow's milk/gluten cause asthma, allergic rhinitis, and chronic sinusitis; gluten and almonds cause throat swelling and asthma exacerbation	After dose 2, patient consumed wheat without throat swelling; after dose 4, patient can now eat gluten, corn, and cow's milk without chronic sinusitis symptoms and asthma; after 6th dose, patient able to eat larger quantities of wheat and cow's milk with only mild allergic rhinitis, asthma, and chronic sinusitis symptoms
JF	M	19	5268	300 mg q. 2 wk	Hops, egg white, oat, salmon, green pea, peanut, banana, cashew nut, coconut, gluten, halibut, honeydew, cow's milk, egg white, and seafood mix	Food allergies (especially cow's milk, gluten, and avocado)—severe chronic atopic dermatitis	After dose 32, moderate improvement in atopic dermatitis despite consuming avocado; after dose 35, major improvement in atopic dermatitis despite consuming gluten and rye
KH	F	36	116	300 mg q. 4 wk	Rye, pear, banana, tuna, scallops, peanut, wheat/rye, soy, shrimp, salmon, oyster, lobster, soybean, crab, olive, nut mix, corn, cow's milk, watermelon, and strawberry	Chocolate/seafood/salmon—associated with anaphylaxis; most other foods listed associated with chest tightness and asthma	After dose 7, patient able to consume shellfish without asthma or anaphylactic reaction

Table 1 Food allergy patients and changes with Xolair (Continued)

Patient Initials	Sex	Age (yr)	Pretreatment Serum IgE Level (kU/L)	Xolair Dose	Skin Test Sensitivity	Allergic Reaction	Efficacy of Omalizumab on Food Allergy
RH	F	53	53	150 mg q. 4 wk	Celery, green pea, salmon, strawberry, avocado, egg whole, mint, mustard, yeast, codfish, haddock, halibut, cashew, pecan, cinnamon, malt, mint, parsley, peach, banana, wheat, corn, walnut/tree nuts, seafood mix, and soy	With all food mentioned, patient develops an itchy mouth and throat, HA, stomach ache, oral allergy, angioedema, asthma; sulfite sensitivity—causes perioral and oral dermatitis	After dose 2, patient able to eat hazelnuts without oral allergy symptoms; after dose 5, patient able to eat hazelnut and coconut without asthma or angioedema; after dose 11, patient able to eat additional foods (egg and mint) without oral allergy symptoms
LH	F	26	301	300 mg q. 2 wk	Wheat/rye, peanut, soybean, and cow's milk	Atopic dermatitis, GERD, asthma, GI/IBS symptoms, and CRS	After dose 11, atopic dermatitis, IBS symptoms, asthma, and chronic sinusitis all improved despite consumption of soybean, cow's milk, and green peas
DM	F	62	503	300 mg q. 2 wk	Tomato, apple, potato, orange, and pork	All foods cause asthma exacerbations and angioedema	After dose 10, patient able to ingest tomatoes, potatoes, and orange without angioedema or asthma exacerbation
CM	F	41	444	300 mg q. 4 wk	Soybean, corn, tree nuts, peanut, and seafood	Chronic sinusitis, GERD/gastritis, and migraine HA	After dose 6, HA and GI/IBS resolved despite consuming corn and soybean
DR	F	66	60	150 mg q. 4 wk	Seafood mix, tree nut mix, corn, and peanut	Chronic sinusitis (CRS), and GERD/gastritis/IBS	After dose 6, patient can ingest corn, peanut butter, and orange juice without CRS or GI symptoms

Table 1 Food allergy patients and changes with Xolair (Continued)

Patient Initials	Sex	Age (yr)	Pretreatment Serum IgE Level (kU/L)	Xolair Dose	Skin Test Sensitivity	Allergic Reaction	Efficacy of Omalizumab on Food Allergy
AS	F	48	239	150 mg q. 2 wk	Pineapple, halibut, pork, barley, beef, grapefruit, white fish, crab potato, lobster, milk, shrimp, and wheat	Chronic sinusitis (CRS), GERD/gastritis/IBS, and HA.	After dose 9, patient able to eat without GI symptoms
MT	F	17	618	300 mg q. 4 wk	Walnut, egg white, seafood mix, tree nut, wheat/rye, soybean, peanut, shrimp, celery, cow milk, corn, orange, and tomato	Chronic sinusitis, GERD/GI symptoms, angioedema associated with peanut, celery, and cantaloupe	After dose 4, patient tolerated peanuts without nasal or ocular symptoms; after dose 6, patient has eaten peanut butter without angioedema and anaphylaxis; after dose 35, shrimp did not cause anaphylaxis
MT	M	15	1813	300 mg q. 4 wk	Shrimp, lobster, crab, tuna, salmon, codfish, and almonds	Urticaria, GI/IBS symptoms, and anaphylaxis	After dose 24, patient consumed almonds without anaphylaxis; after dose 25, patient able to eat fish without anaphylaxis; after dose 28, patient could eat fish and almonds without GI symptoms or anaphylaxis

AD = atopic dermatitis; CRS = chronic rhinosinusitis; GERD = gastroesophageal reflux disease; GI = gastrointestinal; HA = headache; IBS = irritable bowel syndrome;

had concomitant food allergies. The patients' allergic reactions to sensitized foods were compared before and after omalizumab treatment.

METHODS

Patients

Patients were selected if they were treated with omalizumab for moderate to severe persistent asthma, had a history of an allergic food reaction, were skin-prick test (SPT) positive to foods, and had unintended consumption of these sensitized foods while on omalizumab. Twenty-two patients who met these criteria were included in the study from a total of 82 patients treated with omalizumab for asthma (see Table 1).

Study Design

An Institutional Review Board–approved prospective study was performed. All patients in a private allergy/clinical immunology practice clinic on omalizumab were reviewed when they came into the office for their omalizumab injection. All patients received therapy with omalizumab for at least a 1-year duration. Of these patients, those who were SPT⁺ to foods were selected. These SPT⁺ patients were then reviewed for a history of a reaction to their SPT⁺ foods. Those patients who had a positive history of an allergic reaction to their SPT⁺ foods were selected. Finally, these patients were further analyzed to determine if they had an unintended food consumption or unauthorized deliberate food consumption while on omalizumab. Symptoms and severity of allergic reactions were recorded before and after being on omalizumab. Assessment of clinical changes and adverse effects were made at every bimonthly or monthly patient visit. These assessments included vital signs, full physical examination, detailed history of foods consumed, and any possible food allergy incidents.

Drug

Standard therapy with omalizumab was given based on body weight in kilograms and pretreatment serum IgE levels. Doses were 150 or 300 mg subcutaneously given monthly or bimonthly. All patients remained in the clinic 90 minutes after their omalizumab injections to observe for systemic reactions. All patients were dispensed an Epi-pen (Meridian Medical Technologies, Inc., Columbia, MD) and were educated on its use. Patients continued on their other prescribed allergy and asthma medications including immunotherapy.

Skin-Prick Tests

Patients were given SPTs to multiple allergens including cow's milk, egg, codfish, wheat, soy, shrimp, and peanut. In addition, other foods were selected

based on history and tailored to each individual patient. SPTs were performed by skilled nursing personnel. Positive tests were counted as wheals of >3 mm in diameter after 20 minutes. Tests were compared with positive histamine controls and negative saline controls. Commercial extracts used were manufactured by Hollister-Stier (Spokane, WA) and Greer Laboratories (Lenoir, NC). No intradermal testing was performed.

RESULTS

In this private practice clinic, 82 patients were on omalizumab. Of those 82 patients, 46 patients had a positive SPT and a positive food-allergic history. Of those 46 patients, 22 of them had unintended or unauthorized deliberate consumption of their allergic food while on omalizumab. These 22 patients were further analyzed.

Thirteen were female patients and nine were male patients. Age range was 14–66 years old with a mean of 38 years. Mean IgE level was 1120.74 IU/mL. Sensitized allergens included fish, shellfish, peanut, tree nuts, egg, soybean, wheat, and multiple other foods. All 22 (100%) patients maintained significant improvement by history as shown by a decrease or absence of clinical symptoms on accidental or intentional reexposure to sensitized foods. Clinical improvement by the sixth dosage of omalizumab was noted (on average) by history and physical examination (see Table 1).

The symptoms of the allergic food reactions were highly variable. They included 8 patients who noted a decrease in their food-induced atopic dermatitis while on omalizumab, 13 patients who noted a decrease in their food-induced asthma symptoms while on omalizumab, 3 patients who noted a decrease in their food-induced urticaria while on omalizumab; 8 patients who noted a decrease in their food-induced rhinosinusitis symptoms while on omalizumab, and, finally, 9 patients who demonstrated reduced systemic symptoms such as angioedema associated with their food allergy while on omalizumab.

DISCUSSION

All 22 patients in this study reported a decrease or absence of their food allergies while receiving omalizumab. Two factors need to be considered. First, the amount of food ingested in this study was not a controlled amount as would be expected in a physician-directed oral challenge. Therefore, it is difficult to know how much of the food the patients consumed. If the patient had consumed more of the allergic food, perhaps a more severe allergic reaction would have occurred. However, each patient consumed enough food allergen to be aware of their consumption and noticed an improvement when compared with their usual reaction to a similar amount of food.

The second factor to be considered is that this study was not a blinded challenge. Therefore, the patients may have assumed their food allergies would improve while on anti-IgE therapy. This placebo-type effect could have accounted for the decrease in their specific food reactions.

The main side effects of omalizumab are local injection site reactions, viral infections, upper respiratory infection, sinusitis, and headaches. Omalizumab may be also associated with a slight increase in malignant neoplasms (0.5% of patients on omalizumab versus 0.2% of control patients).¹¹ Finally, omalizumab itself has been associated with anaphylaxis that can occur up to 48 hours after injection and, recently, black box warnings have been placed on the medication. The amount of time a patient is observed in the physician's office after omalizumab administration has been increased to 2 hours to minimize this risk. Also, all patients are educated on the possibility of anaphylaxis, the symptoms of anaphylaxis, and the treatment of anaphylaxis. All patients should be given an epinephrine pen to carry with them on their omalizumab injection days.¹² These potentially adverse effects must be considered when considering omalizumab for the treatment of food allergies.

In consideration of omalizumab for food allergies double-blind placebo-controlled studies are needed. However, this will be difficult because of the safety concerns of oral challenges and the risk of anaphylaxis from omalizumab. There has been one published study of anti-IgE for the treatment of food allergies with oral challenges. This study in 2003 was published in the *New England Journal of Medicine* and looked at TNX-901, an anti-IgE medication that is no longer available.¹³ The study had 23 patients on placebo, 59 patients on varying doses of TNX-901. The study concluded that the 450-mg dose of TNX-901 significantly increased the threshold of sensitivity to peanuts on oral food challenge from 178 mg (about one-half of a peanut) to 2627 mg (almost nine peanuts).

This study is similar in its findings to the data in our series. Anti-IgE is shown in both of these studies to increase a food-allergic patient's threshold to their sensitized food and therefore potentially prevent a severe allergic reaction. A small change in tolerability from one-half of a peanut to nine peanuts can make a significant difference in decreasing systemic reactions.¹³

CONCLUSION

While treating asthma patients with omalizumab, patients subjectively observed a reduction in their concomitant IgE-mediated food allergy symptoms. Omalizumab appeared to decrease food sensitivity to various food allergens including cow's milk, egg, codfish, wheat, soy, shrimp, peanut, and tree nuts. The observed effect on food allergies is interesting and further studies are needed. However, for patients who are at significant risk of severe or fatal food anaphylaxis, omalizumab may have a therapeutic role.

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