
Correspondence

MORE THERAPEUTIC ALTERNATIVES FOR CHRONIC IDIOPATHIC URTICARIA?

To the Editor: In relation to the CME Review on therapeutic alternatives for chronic urticaria recently published in *The Annals*,^{1,2} we would like to add some information on another alternative therapeutic approach. From a recent review of the literature (updated November 30, 2007) it emerges that more than 3,000 patients with chronic idiopathic urticaria (CIU) have been studied for antithyroid antibodies (ATA). The prevalence of ATA in CIU seems to vary from 1% to 29% (higher in women in all the studies); in most studies, however, it is significantly higher in patients with CIU than in control patients or in the general population. Our recent figures obtained in more than 500 patients (presented at the 2007 World Allergy Congress held in Bangkok) are 33% in women and 15% in men ($P < .001$). Some authors³ report the prevalence of ATA to be significantly more elevated in patients classified as having autoimmune urticaria on the basis of the results of both the autologous serum skin test and the in vitro histamine release assay.

Considering this close association, other authors attempted to verify whether treatment with thyroxine of either euthyroid or hypothyroid patients with CIU is able to control the symptoms of urticaria, particularly in euthyroid cases, in which the conventional therapeutic approach had been unsuccessful or poorly effective. Although it must be emphasized that the evidence is limited to anecdotal reports and that there is no randomized controlled trial published yet, 101 euthyroid or hypothyroid cases have been evaluated and reported by different authors, and a beneficial effect was observed in a substantial proportion (from 13% to 100%).

We observed no beneficial effect of thyroxine treatment on symptom scores of 46 hypothyroid cases. We therefore agree with the recently published British Society for Allergy and Clinical Immunology guidelines for the management of chronic urticaria and angioedema,⁴ which state that if there is a clear rationale for treating the hypothyroid state with thyroxine, the use of thyroxine in a euthyroid subject is controversial and not recommended. Nevertheless, we believe that this topic should have been discussed.

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Author Response: We thank Dr Zauli et al for bringing up the issue of treating chronic urticaria (CU) associated with thyroid autoantibodies. As stated in the second part of our review,¹ space limitations did not permit us to add sections on CU associated with specific circumstances, eg, infections (*Helicobacter pylori*), hematologic disorders (Schnitzler syndrome), and endocrinopathies (thyroid autoimmunity).

On the subject of CU with thyroid autoantibodies, most authorities agree that a higher prevalence of thyroid autoantibodies is found in patients with CU, although the reported prevalence varies.^{2,3} Most of the controversy centers on therapy for patients with CU and thyroid autoantibodies. In general, the best outcomes seem to be for euthyroid patients with thyroid autoantibodies, who use exogenous levothyroxine at suppressive doses (ie, thyrotropin, 0.50–2.00 mU/L), or for hyperthyroid patients, who take methimazole.⁴

Another unanswered question is whether patients with CU who are euthyroid and without laboratory markers of thyroid autoimmunity should undergo trials of levothyroxine. Currently, evidence does not support this approach,⁵ and, therefore, exogenous levothyroxine should not be considered an alternative therapy for the general CU population.

As with the variety of alternative therapies discussed in our review,^{1,6} at this time, it is left to individual physicians to determine which approaches to include in their therapeutic armamentarium. In patients with CU and thyroid autoantibodies and other patient subsets, additional diagnostic testing must also be considered in the clinical algorithm. Finally, a question that we believe has not been addressed is experience describing treatment of patients with CU and thyroid autoantibodies with the various alternative agents discussed in our review.^{1,6} In common with all other therapeutic considerations, thyroid suppression has a certain failure rate. For patients with CU and thyroid autoantibodies not responding to thyroid suppression, physicians should consider trials of the alternative agents used in the general population of patients with refractory CU.

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OMALIZUMAB AS A THERAPEUTIC ALTERNATIVE FOR CHRONIC URTICARIA

To the Editor: We read the review by Morgan and Khan about therapeutic alternatives for chronic urticaria¹ and would like to report the response to omalizumab in 2 patients with urticarial vasculitis and discuss recent case reports published about the utility of omalizumab in different forms of chronic urticaria.

Omalizumab is a recombinant humanized monoclonal anti-IgE antibody approved for the treatment of moderate to severe persistent asthma by binding to the C3 domain of the heavy chain of IgE.² Omalizumab has been shown to produce immune-modulating effects beyond IgE and its receptors, including effects on peripheral eosinophils by induction of their apoptosis and T-lymphocyte function with down-regulation of the cytokines interleukin 2 and interleukin 13.³ The effects on inflammation in other conditions such as urticaria, including cold urticaria,⁴ chronic urticaria,⁵ cholinergic urticaria,⁶ and idiopathic angioedema,⁷ have been described. We present 2 cases of severe, recurrent normocomplementemic urticarial vasculitis with low serum IgE levels that resolved soon after the initiation of omalizumab therapy.

Patient 1 is a 60-year-old woman with a diagnosis of normocomplementemic urticarial vasculitis made 5 years earlier. Laboratory data were within normal limits. IgE levels were also normal (47.4 kU/L; reference range, 0–180 kU/L). She was treated with different antihistamines and a combination of hydroxychloroquine, leukotriene receptor antagonist, methotrexate, cyclosporine, monthly immunoglobulins, and corticosteroid without response. In this situation, 300 mg of subcutaneous omalizumab was administered. After the first injection skin lesions cleared up completely, the patient has remained free of symptoms for more than 16 weeks; she has tolerated tapering of her oral steroids and continues taking antihistamines.

Patient 2 is a 30-year-old woman with a diagnosis of urticarial vasculitis made 3 years earlier. Her IgE level was 58.6 kU/L (reference range, 0–180 kU/L). She was also treated with different antihistamines and a combination of hydroxychloroquine, leukotriene receptor antagonist, methotrexate, cyclosporine, monthly immunoglobulins, and corticosteroid without response. Despite this, the patient has had multiple visits to the emergency department for relapses of her condition and has received high doses of corticosteroids. In this situation, 300 mg of subcutaneous omalizumab was given. After the first injection skin lesions cleared up completely, the patient has remained free of symptoms for more than 12 weeks; she has tolerated tapering of her oral steroids and continues taking antihistamines.

In conclusion, we think that in the case of refractory urticaria omalizumab might be considered a therapeutic option.

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COMMERCIAL AIRLINES AND FOOD ALLERGY

To the Editor: Regarding the article entitled “Allergic Reactions to Peanuts, Tree Nuts, and Seeds Aboard Commercial Airlines,”¹ please allow me to clarify 2 pieces of information mentioned by the authors, one concerning the Americans With Disabilities Act (ADA) and the other concerning domestic airline policies protecting food allergic passengers.

Although it is true that domestic air carriers cannot discriminate against passengers with disabilities, the mandate stems not from the ADA but rather from the Air Carrier Access Act (ACAA). A precursor to the ADA is section 504 of the Rehabilitation Act of 1973, which prohibits discrimination against individuals with disabilities by any program or activity that receives federal funds. In 1986, the US Supreme Court held that commercial air carriers were not subject to the antidiscrimination requirements set forth under section 504 because they do not receive federal financial assistance.² In response to the US Supreme Court decision, the US Congress passed the ACAA in 1986 to provide a legal cause of action against domestic air carriers that discriminate against passengers on the basis of disability. The ADA was not created by the US Congress until 1990. Its purpose was to expand the prohibition on disability discrimination to employment venues, public programs and services, and private services and facilities. Airlines are expressly exempted from the ADA.

The claim that few domestic carriers have policies protecting food allergic passengers is slightly misleading. Most major domestic airlines have adopted policies to accommodate peanut allergic passengers, and many of these policies are posted on the airline Web sites. Many airlines have stopped serving individual packages of peanuts. Some will serve a nonpeanut snack (such as pretzels) to all passengers on advance request. Others may create a peanut-free “buffer zone” around a peanut allergic passenger. Some will allow a peanut allergic individual to preboard the aircraft and inspect his or her seating area for peanut residue. Some will make an announcement on board the aircraft asking fellow passengers to refrain from eating peanuts they may have brought on board with them. However, peanut allergic passengers often complain about inconsistent application of these policies.

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Erratum

In the article “Relative oral corticosteroid-sparing effect of 7 inhaled corticosteroids in chronic asthma: a meta-analysis” by Anwar K. Abdullah, MD, and Salman Khan, MD (*Ann Allergy Asthma Immunol.* 2008;101:74–81) some words nec-

essary to define n1 and n2 were missing in the legend of Table 2. The legend should read “respectively; n1 and n2, number of patients *who eliminated use of OCS* in the ICS and placebo groups.”