

Revisiting recurrent acute rhinosinusitis prevention by azithromycin in children



To the Editor:

This is in reference to a very well written article titled “Recurrent acute rhinosinusitis prevention by azithromycin in children with nonallergic rhinitis” by Veskitkul et al.¹ The authors have designed a good study and I must commend the authors for their effort. However, there are certain points of concern that I would like to highlight through your esteemed journal.

There have been many studies and reviews that have concluded that antibiotics for recurrent acute rhinosinusitis are unnecessary and not indicated.² Even though the authors have highlighted the issue of growing bacterial resistance to antibiotics, there are a few studies that have reported that patients with recurrent acute rhinosinusitis are prone to develop infection by organisms having increased antimicrobial resistance.³ In such a scenario, it would be prudent to use antibiotics judiciously. In addition, azithromycin is known to have an anti-inflammatory action⁴ and the beneficial effect seen in the azithromycin group may be due to this effect.

The authors have highlighted the underlying immune deficiency in these patients. However, there are studies that have stressed that patients with recurrent acute rhinosinusitis have increased sinonasal anatomical abnormalities such as Haller cells.⁵ In these patients, long-term antibiotics may not help, till the anatomical variations are corrected.

With the increasing resistance to antibiotics and limited armamentarium to fight infections, it is necessary to use antibiotics judiciously. As such we must explore other treatments for the management of recurrent acute rhinosinusitis.

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Reply



To the Editor:

We appreciate the comments by Bakshi,¹ regarding our study titled “Recurrent acute rhinosinusitis prevention by azithromycin in children with nonallergic rhinitis.”²

We agree that antibiotics should be used judiciously in acute rhinosinusitis (ARS) and recurrent acute rhinosinusitis (RARS). A systematic review by Kaper et al³ could not find qualified studies to answer whether short-course antibiotic compared with placebo was effective in RARS in adult patients. As such, the recent International Consensus Statement on Allergy and Rhinology: Rhinosinusitis suggested that “uncomplicated ARS in patients with RARS should be prescribed antibiotics based on the same criteria used to manage primary or sporadic episodes of ARS.”⁴ For children, the guideline by Wald et al⁵ and Fokkens et al⁶ recommended that antibiotic therapy be considered the first-line treatment for ARS in children. The aim of our present study was to evaluate the effect of azithromycin prophylaxis in preventing RARS episodes in children with nonallergic rhinitis.² We found that the ARS episodes in the treatment group decreased significantly and therefore decreased the use of antibiotic for ARS episodes.

For RARS, investigations for underlying causes such as computed tomography scan of the sinus and allergic and immunologic workup are suggested. These investigations are performed in our institute. In cases with underlying diseases that should be treated with surgical management such as adenoid hypertrophy or obstruction of osteomeatal complex from nasal polyp or anatomical abnormalities, the patients are referred to the ENT department for appropriate management. However, the timing for sinus surgery in small children is concerning to both parents and physicians.

The studies of sinus surgery in RARS are limited on small sample sizes and most studies were done in adults.^{4,7} Moreover, the children with RARS in our institute had the age of onset 4.0 ± 1.4 years, making the stepwise medical therapy a more attractive option than sinus surgery.⁸

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Icatibant for ACE-inhibitor angioedema, an opportunity to treat the patients?



To the Editor:

Icatibant was no more effective than placebo in treating at least moderately severe ACE-inhibitor (ACE-I)-induced angioedema in a phase III trial as reported by Sinert et al.¹ However, in this study, more than 90% of the subjects received corticosteroids, antihistamines, or epinephrine before the study drug, and the time to onset of symptom relief was 2 hours in the placebo group. This rapidly favorable outcome of patients in the placebo group (who received antihistamines and/or corticosteroids in a large majority of cases), contrary to all descriptions of bradykinin angioedema, may lead to the mistaken inclusion of histamine-mediated angioedema and explain the absence of a difference. Moreover, the expertise in the diagnosis of ACE-I angioedema of the investigators in this trial was limited. Indeed, 31 centers were needed to include 121 patients, whereas in our study, 4 centers were sufficient to include 62 patients.² Our prospective, multicentric, observational study reported the severity of ACE-induced angioedema and the feasibility of centralization of advices requested by emergency physicians for patients presenting with ACE-induced angioedema, to optimize diagnosis and follow-up.² The call center has already been set up for hereditary patients and has featured in a publication, which indicates feasibility.³ Despite the severity of the cases in our study of ACE-I angioedema, response to treatment with the specific agents plasma-derived C1-inhibitor and icatibant was favorable. We think that a therapeutic trial is possible to demonstrate the efficacy, on morbidity, of icatibant treatment for severe ACE-induced angioedema attacks, the diagnosis of which will be confirmed prospectively and jointly by an angioedema expert, compared with the placebo.

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Reply



To the Editor:

We thank Javaud et al.¹ for their insightful comments on our phase III study² and appreciate the opportunity to respond.

Javaud et al describe positive findings from their group's observational study published in 2015,³ in which 62 patients with angiotensin-converting enzyme (ACE) inhibitor-induced angioedema attacks visiting 1 of 4 emergency departments in Paris were diagnosed with the aid of a centralized call center linking emergency physicians with experts in diagnosing bradykinin-mediated angioedema. They reported a significantly shorter median time from drug administration to onset of symptom relief in patients receiving icatibant or plasma-derived C1 inhibitor versus no specific treatment (0.5 vs 3.9 hours, respectively; $P < .0001$).³ These findings are encouraging but should be interpreted within the context of clear study design limitations, including the absence of a control group and the likelihood of multiple confounders between patients receiving treatment and those not receiving treatment. Moreover, and in direct contrast to our study, Javaud et al did not include a standardized measure for patient reassessment and there is likely to have been inherent variability in subjective determination of symptom relief. The fact that more than half of the 27 patients admitted to the hospital were discharged within 24 hours, only 2 were admitted to the intensive care unit, and just 1 was intubated also raises questions about the purported severity of cases included in their cohort.

With regard to Dr. Javaud's suggestion of a lack of diagnostic expertise in our phase III study, we appreciate the potential benefits of a centralized call center providing expert assistance with diagnosing ACE inhibitor-induced angioedema, particularly in a country like France where emergency medicine is not a recognized specialty and dedicated residency training does not exist. However, nearly all patients in our study were enrolled at academic medical centers in the United States, United Kingdom, and Canada, where a rigorous board certification process for emergency physicians exists, ensuring that clinicians involved in our study were adequately qualified to recognize the presence of this condition without such support. It is, of course, possible that our study population inadvertently included some patients with histamine-induced angioedema (as may have occurred in Dr.

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