

Corresponding author: İnsu Yılmaz, MD, Erciyes University School of Medicine, Department of Chest Diseases, Division of Immunology and Allergy, 38039 Melikgazi, Kayseri, Turkey. E-mail: insu2004@yahoo.com.

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Recurrent acute rhinosinusitis prevention by azithromycin in children with nonallergic rhinitis—don't extrapolate



The study by Veskitful et al¹ examined the benefit of azithromycin in preventing recurrent acute sinusitis in a select group of children. Specifically, allergic rhinitis was excluded from the study, and 80% of the children had low immunoglobulin subclasses. They describe fewer reports of rhinosinusitis exacerbations among the 20 randomly assigned to receive azithromycin than were seen in the placebo group.

I have 2 concerns regarding this study. First, rhinosinusitis exacerbations were defined as: (1) symptoms of an upper respiratory infection (URI) lasting more than 10 but less than 30 days, (2) worsening symptoms of a URI after initial improvement, or (3) severe symptoms at onset defined as purulent nasal discharge for 3 to 4 days with high fever. Symptoms identified as being from a URI were not defined. Moreover, there is a substantial difference in clinical concern between exacerbations characterized by definitions 1 and 3. Which of the specific symptoms indicating an exacerbation were present, and which were noted to differ between the treated and placebo patients?

A second concern is the unusual characteristics of the patient population studied. Why were immunoglobulin subtypes examined in these patients, and what are the implications of those findings in 80% of the patients? Further immune evaluation appears to be indicated in those patients.

There is already a reason for concern regarding overuse of antibiotics for acute rhinosinusitis by well-intentioned physicians following what they perceive as current guidelines.² It is imperative that the current study should not be used to encourage the use of azithromycin for prevention of recurrent rhinosinusitis in children without addressing the specific concerns described above.

Miles Weinberger, MD

University of California San Diego, Rady Children's Hospital, San Diego, Calif.

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Corresponding author: Miles Weinberger, MD, 450 Sandalwood Court, Encinitas, CA 92024. E-mail: miles-weinberger@uiowa.edu.

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Reply



To the Editor:

We appreciate the comments by Professor Weinberger¹ regarding our study titled "Recurrent acute rhinosinusitis prevention by azithromycin in children with nonallergic rhinitis."²

In our present study, the diagnosis of acute rhinosinusitis (ARS) was defined by the American Academy of Pediatrics' criteria as follows: persistent symptoms of an acute upper respiratory tract infection (URI), worsening symptoms of a URI, or severe symptoms.^{3,4} Recurrent acute rhinosinusitis (RARS) was defined as 3 episodes of ARS in 6 months or 4 episodes in 12 months, each lasting <30 days and separated by intervals of ≥10 days during which the patient was asymptomatic.^{3,4} In this study, the presenting symptoms of RARS in azithromycin versus placebo group were purulent nasal discharge 100% versus 100%, nasal congestion 100% versus 95%, postnasal drainage 70% versus 45%, and facial pain 0% versus 10%, $P > .05$. The criteria used to diagnose ARS in azithromycin versus placebo group were persistent symptoms 55.9% versus 51.3%, worsening symptoms 35.3% versus 35.9%, and severe symptoms 8.8% versus 12.8%, $P > .05$.

RARS and chronic rhinosinusitis (CRS) are uncommon conditions in healthy children. The investigations for underlying causes such as allergic rhinitis, immunologic workup, and computed tomography scan of the sinus are suggested.⁵ Shapiro et al⁶ studied 61 children with CRS referred to an allergist for allergy and immunology workup. They found that 36% of subjects had a positive skin test result to inhalant allergen and 56% had low IgG or a poor antibody response to a polysaccharide vaccine or both.⁶ Veskitkul et al⁷ found that the most common predisposing factor for RARS in children was a deficiency in an IgG subclass (78.7%), followed by nonallergic rhinitis (64.9%) and allergic rhinitis (35.1%). In our present study, most patients had a deficiency in an IgG subclass that did not justify monthly use of intravenous immunoglobulin.² The practice parameter for the diagnosis and management of primary immunodeficiency suggests that milder antibody deficiencies (eg, selective deficiency of IgA, deficiency of an IgG subclass, deficiency of a specific antibody, or transient hypogammaglobulinemia of infancy) can be treated with antibiotic prophylaxis.⁸

We agree that antibiotics should be used judiciously in children with RARS. The underlying causes should be identified and specific treatment should be done before starting antibiotic

prophylaxis in these children. We excluded children with allergic rhinitis in this study because the specific treatment is immunotherapy.

Jittima Veskitkul, MD
Orathai Jirapongsananuruk, MD

Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.

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Corresponding author: Orathai Jirapongsananuruk, MD, Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University, 2 Prannok Rd, Bangkoknoi, Bangkok 10700, Thailand. E-mail: orathai.pib@mahidol.ac.th, jirapongo@yahoo.com.

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Anxiety and asthma in inner-city black adolescents: What could be the underestimated, possible connection?



To the Editor:

We read with interest the excellent article by Shams et al¹ reporting that about one-third of inner-city black adolescents with persistent asthma may have anxiety disorders associated with poor asthma control. However, they did not provide comments on the causal and temporal association between anxiety and asthma outcomes. Therefore, we would like to suggest some potential mechanisms to explain the correlation between stress/anxiety and asthma in black adolescents.

In this journal we² have previously shown that about 63% of patients with asthma reported the usual appearance of at least 1 nonrespiratory symptom (n-RS) before an asthma attack. Anxiety, and to a lesser extent depression, represented the most common n-RSs in our study, suggesting that both anxiety and depression may have a possible role in the development and trigger of an asthma attack. Several studies have shown that psychological stress may enhance bronchial hyperreactivity through several

mechanisms, while others established a significant relationship between psychosocial stress and stimulation of the cholinergic system, which could be responsible for the increased airway resistance.

It is likely that some symptoms induced by abnormal cholinergic tone, such as those induced by psychological stress, could be presented together with parasympathetic-associated respiratory symptoms. Therefore, we suggest that attention should be focused on the potential role of the parasympathetic system as a trigger of bronchial obstruction in adolescents with asthma who report the usual onset of cholinergic-related n-RSs (ie, stress and/or anxiety) before an asthma attack. Indirectly, the results of our study confirmed the assumption that cholinergic pathway is a determinant bronchoconstrictor, at least in a specific group of patients with asthma.^{3,4}

The vagal hyperactivity induced by anxiety and stress in patients with asthma also represents the basis of important considerations by a therapeutic point of view, such as the use of anticholinergic agents.

Considering this background, we suggest the need of an adequate phenotyping of adolescents with asthma (either black or white) who could exhibit an increased basal cholinergic tone.⁵ The effect of oxygen and methacholine inhalation, neck suction, slow deep breathing assessed by multiple frequency forced oscillation technique as well as measurement of resting heart rate and pupillometry represent the most effective methods for evaluating the level of vagal tone.

In conclusion, the currently available literature indicates that anxiety and related psychological disorders should be considered as mechanisms that might trigger the airway inflammation, the onset of asthma attack, and the severity of respiratory symptoms. Adequate educational programs should be planned for those patients with asthma suffering from psychological disorders. This approach requires a peculiar attention in adolescents to obtain a better control of respiratory symptoms, a delay in asthma progression, and a reduced airway remodeling in the future.

Gennaro Liccardi, MD^{a,b}
Luigino Calzetta, PhD^{b,c}
Manlio Milanese, MD^d
Antonello Salzillo, MD^a
Gerardo Apicella, MD^a
Maria Gabriella Matera, MD^e
Paola Rogliani, MD^{b,c}

^aDepartment of Pulmonology, Haematology and Oncology, Division of Pneumology and Allergology, High Speciality "A. Cardarelli" Hospital, Naples, Italy

^bPostgraduate School of Respiratory Medicine, Department of Experimental Medicine and Surgery, University of Rome "Tor Vergata", Rome, Italy

^cDepartment of Experimental Medicine and Surgery, University of Rome "Tor Vergata", Rome, Italy

^dDivision of Pulmonology, S. Corona Hospital, Pietra Ligure, Italy

^eDepartment of Experimental Medicine, Second University of Naples, Naples, Italy.

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Corresponding author: Gennaro Liccardi, MD, Department of Pulmonology, Haematology and Oncology, Division of Pneumology and Allergology, High Speciality "A. Cardarelli" Hospital, Piazzetta Arenella n° 7, 80128 Naples, Italy. E-mail: gennaro.liccardi@tin.it.

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