Nasopharyngeal Flora in Children on Inhaled Corticosteroid Therapy

We read with interest the recent article by Nirmal, *et al*. [1]. We congratulate the authors for carrying out this study, which definitively clearified some issues related to the long-term use of inhaled corticosteroid (ICS) in children. However, we want to highlight some points related to this article.

In this study, the ratio of the case (n=75) to control (n=25) was only 3:1, which may decrease the statistical power of the study and make a comparison between the groups difficult. For optimal statistical power, at least a 1:1 ratio is suggested. The number of controls rather than cases increase the statistical power, but this effect is negligible after the case to control ratio 1:4 [2].

Allthough it was not the objective of this study to look at fungal colonization, but fungi also form an important component of nasopharyngeal flora. ICS is well known to enhance fungal colonization in naso-oropharynx [3]. Hoarseness of voice and oropharyngeal candidiasis are known side effects of ICS as a result of fungal colonization [4]. Therefore, it would have been interesting if the authors had also considered fungal colonization in this study.

It is essential to look at adherence to ICS therapy since poor adherence might have a nasopharyngeal flora similar to control group. Authors should have given information on adherence to therapy in the study participants.

Authors had mentioned low, moderate and high doses of ICS in children ≥ 6 y; however, they did not describe the same in children < 5 y of age (28 % of the cases).

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AUTHOR'S REPLY

We would like to thank the reviewer for taking interest in our study. In our study, the ratio of the case to control was 3:1. Wacholder, *et al.* [1] have reported that the best way to increase precision in a case-control study is to increase the number of cases by widening the base geographically or temporally rather than by increasing the number of controls because the marginal increase in precision from an additional case is greater than from an additional control.

In a metanalysis done by Rachelefsky, *et al.* [2] ICS metered-dose inhaler (MDI) device was associated with a 5-fold greater risk of oral candidiasis as compared to placebo. Increased risk of fungal colonization has been demonstrated in numerous studies as suggested by the reviewer. As we could not find much literature on the colonization pattern of bacterial flora in asthmatic children on ICS, our study mainly focused on bacterial colonization.

In our study, except three, all the asthmatic children were compliant with the prescribed medicines. None of these three children had colonization of nasopharynx by the pathogenic organisms.

According to GINA guidelines, for children less than 5 years, a low dose of inhaled budesonide with spacer was 200µg and 400µg were considered as double low dose ICS [3]. In asthmatic children younger than 5 y, colonization with pathogenic organism was found in 31% of asthmatic children who were taking low dose ICS as compared to 40% of asthmatic children who were taking double low dose ICS, which was not statistically significant (P = 0.72), but for maintaining uniformity, we considered Double low dose ICS as the medium dose of ICS in our analysis.

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