

Correspondence

***Trichuris suis* might be effective in treating allergic rhinitis**

To the Editor:

We compliment Bager et al.¹ for performing the first randomized, double-blind controlled trial of *Trichuris suis* ova in the treatment of allergic rhinitis. They concluded that the agent had no therapeutic effect on grass pollen-induced disease. Our studies demonstrated that *T suis* exposure reduced disease activity in patients with immune-mediated ulcerative colitis and Crohn disease.^{2,3} Mechanistic studies in animals demonstrated that helminth exposure reduced hyperactive airway disease through induction of regulatory T cells.^{4,5} In the study by Bager et al.,¹ *T suis* ova treatment produced definite biologic effects, including increased eosinophil counts and *T suis*-specific IgE, IgG4, and IgA levels. These observations established that *T suis* had a significant effect on the human immune system. However, several features of the study design and conduct possibly caused the investigators to miss a treatment benefit.

The most important problem with the study was late administration of *T suis* ova with respect to the tree allergy season because it takes time for the helminths to induce clinically significant disease modulation. Subjects were enrolled from March 10 through May 15, and the allergic rhinitis season was from May 28 through July 27, with the peak beginning June 9. Distribution of enrollment dates is not described in detail with respect to the allergy season, but by season peak, some subjects had received only 2 treatments administered 21 days apart, and 23% of subjects were treated for only 3 to 5 weeks. Thus many subjects were treated too late for therapeutically apparent effects by season peak. In our studies clinical effects were not apparent until 6 weeks.² *Post hoc* analysis of those patients treated for 6 to 15 weeks increases type 2 error.

Subject characteristics were similar except that severity of allergic rhinitis was greater in the *T suis* ova-treated group (moderate-severe, 94%; mild, 6%) than in the placebo-treated group (moderate-severe, 82%; mild, 18%). Differences in severity might have skewed the results against the *T suis* ova-treated subjects, particularly when combined with incomplete *T suis* exposure at peak season.

Although the primary change in symptom score demonstrated no difference between *T suis* ova- and placebo-treated subjects, other parameters were statistically significant or showed a definite

trend in favor of *T suis* ova. Medications used were 31 tablets (29% days) with *T suis* ova versus 45 tablets (35%) with placebo ($P = .04$), and mean daily medication scores were less with *T suis* ova (4) than with placebo (5.1, $P = .11$). There was little comment about these results and no discussion that higher use of antihistamines might have reduced the symptom score in the placebo-treated subjects.

Thus it is premature to conclude that *T suis* ova had no therapeutic effect for treatment of grass pollen-induced allergic rhinitis.

Bager et al.¹ report that some *T suis* ova-treated subjects had transient diarrhea around 30 to 50 days of treatment. However, diarrhea was not statistically different than in the placebo group. In our studies we used authenticated tools to measure stool patterns and saw improvement in diarrhea.² In the study by Bager et al.,¹ subjects did not spontaneously report diarrhea, and the severity and duration was not described. Therefore it is difficult to determine whether this description is clinically significant.

Robert W. Summers, MD^a

David E. Elliott, MD, PhD^a

Joel V. Weinstock, MD^b

From ^aDepartment of Internal Medicine, the University of Iowa Carver College of Medicine, Iowa City, Iowa, and ^bDepartment of Internal Medicine, Tufts–New England Medical Center, Boston, Mass. E-mail: david-elliott@uiowa.edu.

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