

Anti-fungal drug offers great benefits to some with severe asthma

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Some patients with severe asthma who also have allergic sensitivity to certain fungi enjoy great improvements in their quality of life and on other measures after taking an antifungal drug, according to new research from The University of Manchester in England.

The findings were reported in the first issue for January of the American Thoracic Society's *American Journal of Respiratory and Critical Care Medicine*.

"We knew that many people with severe asthma are sensitized to several airborne fungi which can worsen asthma without overt clinical signs. The question was: does antifungal therapy provide any clinical benefit," said David Denning, F.R.C.P., F.R.C.Path., professor of medicine and medical mycology at The University of Manchester and lead investigator of the study.

In 2006, the most recent year for which official statistics are available, there were more than 16 million adults with self-reported asthma in the U.S.; about 20 percent of them have severe asthma.

A small number of severe asthmatics—about one percent— are known to have a syndrome called allergic bronchopulmonary aspergillosis, an extreme allergy to *Aspergillus fumigatus* fungus that is associated with the long-term colonization of their respiratory tracts with the fungus. But many more — 20 to 50 percent— are sensitized to a variety of fungi without showing overt clinical signs or demonstrable colonization. It is

these patients with severe asthma with fungal sensitization, or "SAFS", as the researchers named the syndrome, who are most likely to enjoy marked improvement with the antifungal therapy.

In the prospective double-blind study, 58 patients with severe asthma and allergic sensitivity to at least one of seven different common fungi (confirmed by a skin-prick test and/or an IgE blood test for the study) were randomized to receive either an oral dose of itraconazole (200mg twice a day) or a placebo.

After 32 weeks of treatment, 18 of the 29 patients (62 percent) who were randomized to receive the drug experienced significant improvements on their Asthma Quality of Life Questionnaires, and in runny nose and morning lung function. However, 11 of the patients who received the drug left the trial before completion, some citing side effects that included nausea, breathlessness and muscle weakness. Unfortunately, four months after stopping antifungal treatment, symptoms had returned.

"This study indicates that fungal allergy is important in some patients with severe asthma, and that oral antifungal therapy is worth trying in difficult-to-treat patients. Clearly itraconazole will not suit everyone and is not always helpful, but when it is the effect is dramatic," said Dr. Denning. "These findings open the door to a new means of helping patients with severe asthma, and raise intriguing questions related to fungal allergy and asthma."

John Heffner, M.D., past president of the ATS, reflected that the recent Severe Asthma Research Program report describes severe asthma as a entirely different form of the disease. "Patients with severe asthma may have unique triggers for bronchospasm, which remain unidentified. This study suggests that colonization with fungal species may generate immunologic responses in patients with asthma that perpetuate airway

inflammation and blunt the effectiveness of drug therapy. One can't help but wonder if antifungal therapy would benefit all severe asthmatics regardless of sensitivity to fungi."

Source: American Thoracic Society

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