

Management of allergic fungal sinusitis with postoperative oral and nasal steroids: A controlled study

Introduction

In patients with allergic fungal sinusitis, the mainstay of treatment remains surgical removal of allergic mucin and fungal debris. But as a single modality, surgery is associated with high rates of recurrence, so a number of adjunctive medical modalities have been tried, including postoperative corticosteroid therapy. We conducted a study of 63 patients with allergic fungal sinusitis who underwent endoscopic sinus surgery with or without postoperative steroid therapy. A group of 30 patients who had been treated prior to January 2000 had undergone surgery only; their cases were reviewed retrospectively, and they served as historical controls. Another 33 patients who were treated after June 2000 underwent surgery plus oral and nasal steroid therapy. All patients were followed for a minimum of 2 years. Recurrences were seen in 50.0% (15/30) of the no-steroid group and 15.2% (5/33) of the steroid group—a statistically significant difference ($p = 0.008$). The results of our study strongly support the use of steroids to control allergic fungal sinusitis and prevent its recurrence, and we recommend further study to identify the optimal dosage and duration of therapy.

Allergic fungal sinusitis was first described in the early 1980s by Millar et al([n1](#)) in the United Kingdom and by Katzenstein et al([n2](#)) in the United States. The organisms responsible for most cases of this disease are *Aspergillus* spp and members of the family of dematiaceous fungi.([n3](#), [n4](#)) Typically, patients are young and immunocompetent, and they present with a history of atopic disease.

The onset of allergic fungal sinusitis occurs with the inhalation of fungal spores to which the patient is allergic. In response, the sinonasal mucosa produces a copious amount of secretions (mucin), but the process of mucociliary clearance fails to remove the spore. The fungal spore then germinates in the mucin and continues to provide an antigenic stimulus. Polyps and hyperplastic mucosa form as a result of the inflammatory stimulus.

The diagnostic criteria for allergic fungal sinusitis include the presence of nasal polyposis, atopy to fungi, characteristic findings on computed tomography (CT) and magnetic resonance imaging, and a characteristic histopathologic picture in which fungal hyphae are found in eosinophilic mucin without evidence of tissue invasion.([n5](#), [n6](#))

The management of allergic fungal sinusitis is difficult, and treatment failure is common. In fact, recurrence rates as high as 100% have been reported following surgical management.([n5](#), [n7](#)) In an effort to lower the risk of recurrence, the use of postoperative medical treatment with corticosteroids has been tried in various centers worldwide, based on experience with the treatment of allergic bronchopulmonary aspergillosis.([n8](#))

We report our experience in managing patients with allergic fungal sinusitis who had endoscopic sinus surgery with and without adjunctive postoperative steroids.

Patients and methods

The purpose of this study was to determine if the addition of postoperative steroid therapy has any effect on preventing recurrences in patients who undergo endoscopic sinus surgery for the treatment of allergic fungal sinusitis. The study was conducted at the Department of Otolaryngology-Head and Neck Surgery at the Aga Khan University Hospital in Karachi, Pakistan. The study population was drawn from patients who had been diagnosed with allergic fungal sinusitis on the basis of characteristic clinical findings and confirmed by intraoperative findings (mucin and fungal debris) and histopathologic analysis. Exclusion criteria included invasive infection that extended beyond the nose and paranasal sinuses, immunocompromise, failure to participate in regular follow-up, and revision surgery.

This study was conducted in two parts—a prospective phase and a retrospective review. In the prospective phase, we studied 33 patients—21 men and 12 women (mean age: 31 yr)—whose sinusitis was treated with surgery plus steroid therapy (steroid group). For comparison purposes, we reviewed the records of 30 historical controls—16 men and 14 women (mean age: 29 yr)—who met the same inclusion and exclusion criteria and whose sinusitis had been treated with surgery only (no-steroid group). All patients in the no-steroid group had been treated prior to 2000, when it was not the policy of our institution to administer adjunctive postoperative steroid therapy. All patients in the steroid group were treated after June 2000. All 63 patients in this study were operated on in our department by a single surgeon (M. Ikram).

In the steroid group, patients were prescribed postoperative oral prednisone (0.5 mg/kg) for 1 month, followed by topical beclomethasone (2 sprays in each side twice daily) for 5 months. If the appearance of the nasal mucosa was greater than stage 0 as described by Kupferberg et al ([n5](#)) during nasal steroid therapy, a short course of oral steroids at 0.5 mg/kg/day for 1 to 2 weeks was given to restore the mucosa to stage 0.

All patients were followed for a minimum of 2 years. Patients were seen for follow-up once a month for 6 months, then once every 3 months for at least 18 months. At the monthly follow-ups, all patients underwent nasal endoscopy and measurement of their IgE level. All patients were actively encouraged to perform daily nasal lavage with normal saline, which we believe helps clear crust and debris from the nose. All recurrences were treated with revision surgery.

Our data were statistically analyzed with the aid of the Statistical Package for the Social Sciences software (version 13; SPSS; Chicago), and recurrence data were subjected to Kaplan-Meier analysis.

Results

At presentation, most patients had bilateral disease, nasal polyps, nasal obstruction, and headache (table 1).

Allergic fungal sinusitis recurred in 15 of the 30 no-steroid patients (50.0%), compared with only 5 of the 33 steroid patients (15.2%). The difference was statistically significant ($p = 0.008$).

According to the Kaplan-Meier analysis, the probability of treatment response was 0.8 in the no-steroid group (table 2) and 0.9 in the steroid group (table 3). The cumulative probability of

remaining disease-free was 0.4656 in the no-steroid group and 0.8156 in the steroid group (figure, table 2, and table 3).

No patient in the steroid group reported any serious side effects of steroid therapy. Six patients (18.2%) experienced skin spots during the final week of their oral steroid regimen, but these lesions disappeared upon the conclusion of oral therapy.

Discussion

A number of contributing factors are associated with allergic fungal sinusitis. For example, atopy, continuous exposure to antigens, and inflammation all play key roles in the disease and its recurrence.([n9](#))

Historically, all forms of fungal sinusitis were treated with a combination of extensive surgical debridement and medical treatment.([n10](#)) However, in most early reports, allergic fungal sinusitis was not adequately distinguished from other forms of fungal sinusitis, and this made it difficult to compare different treatments.([n11](#))

Ever since allergic fungal sinusitis was first described,([n1](#), [n2](#)) the primary mode of treatment has been surgical resection of allergic mucin and obstructing hypertrophic mucosal disease. More recently, conservative surgical procedures such as endoscopic debridement have been advocated.([n12](#)) Today, in addition to the surgical removal of allergic mucin and fungal debris, treatment includes the creation of patent sinus ostia that are large enough for adequate aeration and drainage of sinuses. But as mentioned, endoscopic sinus surgery is associated with high rates of recurrence.([n5](#), [n7](#)) In an effort to reduce these recurrence rates, researchers have tried various medical therapies as adjunctive treatment, including antifungal agents, immunotherapy, and steroids.

Antifungal agents. The authors of some early reports recommended the use of antifungal drugs,([n13](#), [n14](#)) but no prospective, controlled studies have been conducted to support their use. In fact, in noninvasive fungal disease, the risks associated with these medications may outweigh their benefits.([n15](#)) Ricch-etti et al reported that the use of a topical antifungal (amphotericin B nasal lavage) prevented recurrences in nasal polyposis, but the patients in that study had not been diagnosed with classic allergic fungal sinusitis and the study had no control group.([n16](#)) Therefore, further investigation is needed to confirm their findings.

Immunotherapy. The similarity between allergic fungal sinusitis and allergic bronchopulmonary aspergillosis led to an empiric and theoretical intimation that immunotherapy may be beneficial as a component of treatment of the former.([n8](#)) Mabry et al conducted rigorous investigations and found that patients who had undergone immunotherapy in addition to surgery and postoperative steroid therapy experienced less crusting and less recurrence of nasal polyps.([n17](#), [n18](#)) In a subsequent study of outcomes in 8 patients following the discontinuation of immunotherapy, Mabry et al reported no recurrences during 7 to 17 months of follow-up.([n19](#)) In contrast, Ferguson found that patients on immunotherapy either did not improve or actually worsened.([n20](#)) As a result, more study is needed before immunotherapy can be widely accepted as the primary mode of treatment for allergic fungal sinusitis.

Steroids. The similarity between allergic fungal sinusitis and allergic bronchopulmonary aspergillosis also prompted the use of steroids, and many authors advocate their use. In one early report, Waxman et al outlined this relationship and suggested the use of systemic steroids postoperatively.([n21](#)) Since then, both systemic and topical steroids have been recommended, although the optimal dosage and the duration of therapy remain unclear.([n5](#), [n10](#), [n22-n25](#))

In a study of 26 patients with allergic fungal sinusitis, Kupferberg et al found that steroids were associated with greater improvements.([n5](#)) Likewise, Schubert and Goetz retrospectively analyzed outcomes among 67 patients treated and followed over a period of 8 years.([n11](#)) All patients had been treated similarly with respect to sinus surgery, immunotherapy, anti-inflammatory nasal sprays, and antihistamines. Roughly half of these patients were treated with postoperative oral steroids and the other half were not. The use of oral steroids was associated with greater clinical improvement and a significantly lower incidence of revision sinus surgery.

Kuhn and Javer have advocated a postoperative steroid protocol that begins with oral prednisone at 0.4 mg/kg/day for 4 days.([n22](#)) The dosage is decreased by 0.1 mg/kg/day every 4 days until it is lowered to either 20 mg/day or 0.2 mg/kg/day, whichever is greater. That low dose is continued for 1 month, at which point the dosage is adjusted so that all patients are given 0.2 mg/kg/day. That dose is maintained while patients are followed monthly with nasal endoscopy and measurements of their IgE level. Later, the steroid dosage is again adjusted to maintain the patient's nasal membrane appearance at stage 0. For patients who maintain a stage 0 appearance for 4 months, the dosage of oral steroid is decreased to 0.1 mg/kg/day and a topical steroid is added. If stage 0 continues for 2 more months, then the oral steroid is tapered off completely and the topical steroid is continued for 1 year.

The results of our study strongly support the use of oral and nasal steroids to control allergic fungal sinusitis and to prevent its recurrence. We recommend further study to identify the optimal dosage and duration of therapy.

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Figure. Kaplan-Meier curve shows the cumulative probability of remaining disease-free in the two groups at study's end-0.8156 in the steroid group and 0.4656 in the no-steroid group

[Table 1. Presenting symptoms in the two groups](#)

Unilateral/bilateral disease	No steroid n (%) 11/19(36.7/63.3)	Steroid n (%) 14/19(42.4/57.6)
Nasal polyps	30 (100)	33 (100)
Nasal obstruction	30 (100)	33 (100)
Headache	27 (90.0)	25 (75.8)
Anosmia	13 (43.3)	18 (54.5)

[Table 2. Probability of treatment response and cumulative probability of remaining disease-free in the no-steroid group \(Kaplan-Meier analysis\)](#)

Study day	Patients w/o recurrence n (%)	Probability of response	Cumulative probability
0	30 (100)	1.0	1.0000
150	30 (100)	0.9	0.9666
180	29 (96.7)	0.9	0.9326
270	28 (93.3)	0.9	0.8992
360	27 (90.0)	0.9	0.8658
450	26 (86.7)	0.9	0.7991
540	24 (80.0)	0.9	0.7657
630	23 (76.7)	0.9	0.7323
720	22 (73.3)	0.9	0.6989
810	21 (70.0)	0.9	0.6322
900	19 (63.3)	0.8	0.5656

990	17 (56.7)	0.9	0.5322
1,080	15 (50.0)	0.8	0.4656

[Table 3. Probability of treatment response and cumulative probability of remaining disease-free in the steroid group \(Kaplan-Meier analysis\)](#)

Study day	Patients w/o recurrence n (%)	Probability of response	Cumulative probability
0	33 (100)	1.0	1.0000
450	33 (100)	0.9	0.9696
630	32 (97.0)	0.9	0.9090
810	30 (90.9)	0.9	0.8786
900	29 (87.9)	0.9	0.8483
990	28 (87.9)	0.9	0.8156

[References](#)

[\(n1.\)](#) Millar JW, Johnston A, Lamb D. Allergic aspergillosis of the maxillary sinuses [abstract]. *Thorax* 1981; 36:710.

[\(n2.\)](#) Katzenstein AL, Sale SR, Greenberger PA. Allergic Aspergillus sinusitis: A newly recognized form of sinusitis. *J Allergy Clin Immunol* 1983; 72 (1): 89-93.

[\(n3.\)](#) Michael RC, Michael JS, Ashbee RH, Mathews MS. Mycological profile of fungal sinusitis: An audit of specimens over a 7-year period in a tertiary care hospital in Tamil Nadu. *Indian J Pathol Microbiol* 2008; 51 (4): 493-6.

[\(n4.\)](#) Manning SC, Holman M. Further evidence for allergic pathophysiology in allergic fungal sinusitis. *Laryngoscope* 1998; 108 (10): 1485-96.

[\(n5.\)](#) Kupferberg SB, Bent JP III, Kuhn FA. Prognosis for allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 1997; 117 (1): 35-41.

[\(n6.\)](#) Cody DT II, Neel HB III, Ferreiro JA, Roberts GD. Allergic fungal sinusitis: The Mayo Clinic experience. *Laryngoscope* 1994; 104 (9): 1074-9.

[\(n7.\)](#) Kuhn FA, Javer AR. Allergic fungal sinusitis: A four-year follow-up. *Am J Rhinol* 2000; 14 (3): 149-56.

[\(n8.\)](#) Greenberger PA, Patterson R. Diagnosis and management of allergic bronchopulmonary aspergillosis. *Ann Allergy* 1986; 56 (6): 444-8.

[\(n9.\)](#) Bent JP III, Kuhn FA. Diagnosis of allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 1994; 111 (5): 580-8.

[\(n10.\)](#) Stevens MH. Primary fungal infections of the paranasal sinuses. *Am J Otolaryngol* 1981; 2 (4): 348-57.

[\(n11.\)](#) Schubert MS, Goetz DW. Evaluation and treatment of allergic fungal sinusitis. II. Treatment and follow-up. *J Allergy Clin Immunol* 1998; 102 (3): 395-402.

[\(n12.\)](#) Singh N, Bhalodiya NH. Allergic fungal sinusitis (AFS)-earlier diagnosis and management. *J Laryngol Otol* 2005; 119 (11): 875-81.

[\(n13.\)](#) Frenkel L, Kuhls TL, Nitta K, et al. Recurrent *Bipolaris* sinusitis following surgical and antifungal therapy. *Pediatr Infect Dis J* 1987; 6 (12): 1130-2.

[\(n14.\)](#) Corey JP, Delsupehe KG, Ferguson BJ. Allergic fungal sinusitis: Allergic, infectious, or both? *Otolaryngol Head Neck Surg* 1995; 113 (1): 110-19.

[\(n15.\)](#) Thrasher RD, Kingdom TT. Fungal infections of the head and neck: An update. *Otolaryngol Clin North Am* 2003; 36 (4): 577-94.

[\(n16.\)](#) Ricchetti A, Landis BN, Maffioli A, et al. Effect of anti-fungal nasal lavage with amphotericin B on nasal polyposis. *J Laryngol Otol* 2002; 116 (4): 261-3.

[\(n17.\)](#) Mabry RL, Manning SC, Mabry CS. Immunotherapy in the treatment of allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 1997; 116 (1 ∥: 31-5.

[\(n18.\)](#) Mabry RL, Marple BF, Folker RJ, Mabry CS. Immunotherapy for allergic fungal sinusitis: Three years' experience. *Otolaryngol Head Neck Surg* 1998; 119 (6): 648-51.

[\(n19.\)](#) Mabry RL, Marple BF, Mabry CS. Outcomes after discontinuing immunotherapy for allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 2000; 122 (1): 104-6.

[\(n20.\)](#) Ferguson BJ. Immunotherapy and antifungal therapy in allergic fungal sinusitis. Presented at the annual meeting of the American Academy of Otolaryngic Allergy; Sept. 14, 1993; Minneapolis.

[\(n21.\)](#) Waxman JE, Spector JG, Sale SR, Katzenstein AL. Allergic *Aspergillus* sinusitis: Concepts in diagnosis and treatment of a new clinical entity. *Laryngoscope* 1987; 97 (3 Pt 1): 261-6.

[\(n22.\)](#) Kuhn FA, Javer AR. Allergic fungal rhinosinusitis: Perioperative management, prevention of recurrence, and role of steroids and antifungal agents. *Otolaryngol Clin North Am* 2000; 33 (2): 419-33.

[\(n23.\)](#) Ferguson BJ. What role do systemic corticosteroids, immunotherapy, and antifungal drugs play in the therapy of allergic fungal rhinosinusitis? *Arch Otolaryngol Head Neck Surg* 1998; 124 (10): 1174-8.

[\(n24.\)](#) Schubert MS. Medical treatment of allergic fungal sinusitis. *Ann Allergy Asthma Immunol* 2000; 85 (2): 90-7.

[\(n25.\)](#) Schubert MS. Allergic fungal sinusitis. *Otolaryngol Clin North Am* 2004; 37 (2): 301-26.