

COMPARISON OF RECURRENCE OF ALLERGIC FUNGAL RHINOSINUSITIS AFTER ENDOSCOPIC SINUS SURGERY USING STEROIDS WITH OR WITHOUT ITRACONAZOLE

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Abstract

Background: Allergic Fungal Rhinosinusitis (AFRS) is subtype of chronic rhinosinusitis characterized by hypersensitivity reaction to fungal elements, leading to persistent inflammation and a high recurrence rate after Endoscopic Sinus Surgery (ESS). **Objective:** to compare the recurrence rates, symptom improvement, and quality of life outcomes in AFRS patients receiving postoperative corticosteroids alone versus those receiving a combination of corticosteroids and itraconazole following ESS. **Hypothesis:** The addition of itraconazole to corticosteroid therapy will result in a statistically significant reduction in AFRS recurrence rates and improved symptom control compared to corticosteroids alone. **Materials and Methods:** A randomized clinical trial was conducted at Bahawal Victoria Hospital, Bahawalpur, from July 2023 to December 2024. Patients diagnosed with AFRS based on Bent and Kuhn criteria who underwent ESS were randomized into two groups: Group A (Corticosteroids Only) and Group B (Corticosteroids + Itraconazole). Primary outcomes included recurrence rates at 12 months post-surgery. Secondary outcomes assessed symptom improvement using SNOT-22 scores and quality of life using RSDI scores. Statistical analysis was performed using SPSS version 24.0. **Results:** Baseline characteristics were comparable between groups. The recurrence rate was significantly lower in Group B (10.0%) than in Group A (25.5%) ($p = 0.004$). Group B also demonstrated greater reductions in SNOT-22 (20 vs. 12 points, $p < 0.001$) and RSDI scores (25 vs. 15 points, $p < 0.001$), indicating better symptom relief and quality of life improvement. **Conclusion:** The addition of itraconazole to corticosteroid therapy significantly reduces AFRS recurrence rates and enhances post-surgical symptom relief and quality of life.

INTRODUCTION

Allergic Fungal Rhinosinusitis (AFRS) is a distinct subtype of chronic rhinosinusitis characterized by a hypersensitivity reaction to fungal elements within the sinonasal cavities. This condition is marked by the presence of eosinophilic mucin containing non-invasive fungal hyphae and is associated with type I IgE-mediated hypersensitivity responses. Patients typically present with nasal polyposis, chronic nasal obstruction, and characteristic radiographic findings, including sinus opacification and possible bone remodeling due to expansive sinusitis. AFRS predominantly affects immunocompetent individuals and is more prevalent in warm, humid climates, accounting for approximately 5% to 10% of all chronic rhinosinusitis cases.^{1,2,3}

The cornerstone of AFRS management involves a combination of surgical and medical interventions. Functional Endoscopic Sinus Surgery (ESS) plays a pivotal role by facilitating the removal of allergic mucin, fungal debris, and nasal polyps, thereby restoring normal sinus drainage and ventilation. ESS not only alleviates symptoms but also enhances the efficacy of postoperative medical therapies by improving drug delivery to the sinus mucosa. However, surgery alone is often insufficient, as AFRS has a high propensity for recurrence. Therefore, ESS is typically complemented with adjunctive medical treatments to manage the underlying inflammatory process and prevent disease recurrence.^{4,5,6}

Postoperative medical management is crucial in reducing the risk of AFRS recurrence. Systemic and topical corticosteroids are commonly employed to suppress the underlying eosinophilic inflammation and modulate the immune response.^{7,8} Additionally, antifungal agents like itraconazole have been utilized for their potential to reduce fungal load and exert anti-inflammatory effects. The combination of corticosteroids with itraconazole aims to address both the inflammatory and fungal components of AFRS, potentially leading to improved outcomes. However, the efficacy of this combined approach in preventing recurrence remains a subject of ongoing research.^{8,9,10}

Despite advancements in understanding AFRS pathophysiology and management, the optimal postoperative treatment regimen to prevent disease recurrence is not well-established. While corticosteroids are a mainstay in therapy, the adjunctive use of antifungal agents like itraconazole

has shown promise but lacks definitive evidence from large-scale studies. This uncertainty underscores the need for further research to evaluate the effectiveness of combined corticosteroid and itraconazole therapy in reducing AFRS recurrence rates following ESS.

Objective

Objective of the study was to compare the recurrence rates of AFRS after endoscopic sinus surgery between two treatment groups: one receiving postoperative corticosteroids alone and the other receiving a combination of corticosteroids and itraconazole.

Hypothesis

Addition of itraconazole to standard corticosteroid therapy will result in a statistically significant reduction in AFRS recurrence rates compared to corticosteroids alone.

Materials and Methods

This randomized clinical trial conducted at Bahawal Victoria Hospital, Bahawalpur from July 2023 to December 2024 after taking approval from institutional ethical review committee and informed consent from individual patient. The study aimed to assess the recurrence rates, symptom improvement, and quality of life outcomes in patients with Allergic Fungal Rhinosinusitis (AFRS) undergoing Endoscopic Sinus Surgery (ESS) followed by either corticosteroid therapy alone or a combination of corticosteroids and itraconazole.

The calculated sample size at 5% significance Level, 80% power of test, 40% recurrence rate with steroids only and 20% recurrence rate with Steroid + itraconazole was 47 patients in each group.^{11,12,13} Patients aged 18–50 years diagnosed with AFRS based on Bent and Kuhn criteria, who had undergone primary ESS for AFRS with evidence of allergic mucin and positive fungal cultures were included in the study. Exclusion criteria was invasive fungal sinusitis, immunodeficiency, or chronic systemic illnesses (e.g., uncontrolled diabetes, malignancies), Prior history of systemic antifungal therapy within six months before surgery, Pregnancy or lactation and history of drug hypersensitivity to corticosteroids or itraconazole.

Participants were randomized into two groups, **Group A** patients received postoperative corticosteroid

therapy, including oral prednisolone (starting at 30 mg/day and tapered over six weeks) and intranasal corticosteroid sprays and **Group B patients** in addition to the corticosteroid regimen received oral itraconazole at a dose of 200 mg/day for three months.

All patients underwent standardized ESS performed by experienced otorhinolaryngologist. The procedure included complete removal of allergic mucin, polyp resection, and wide drainage of affected sinuses. Intraoperative findings were recorded, and postoperative care followed a uniform protocol, including nasal irrigation and debridement.

Recurrence rate of AFRS at 12 months post-surgery, defined as symptomatic disease recurrence with radiographic evidence and/or need for revision surgery. Symptom Improvement was evaluated using the Sino-Nasal Outcome Test (SNOT-22), with scores recorded at baseline and 12 months post-surgery.

Quality of Life was also measured using the Rhinosinusitis Disability Index (RSDI), with improvement assessed from baseline to follow-up. Lund-Mackay Score was used for Pre- and post-treatment radiological assessment.

Data was collected by using preformed questionnaire. Baseline demographic and clinical characteristics were recorded. All the data was entered and analyzed by using SPSS version 24.0. Recurrence rates were compared using the Chi-square test. Changes in SNOT-22 and RSDI scores were analyzed using paired t-tests and p -value < 0.05 was considered statistically significant.

Results

Table I: Sociodemographic Profile of Patients

VARIABLE	GROUP A (CORTICOSTEROIDS ONLY)	GROUP B (CORTICOSTEROIDS + ITRACONAZOLE)	P-VALUE
Age (mean \pm SD, years)	34.5 \pm 8.2	33.8 \pm 7.9	0.56
Gender (male/female)	32/47	28/47	0.62
BMI (mean \pm SD, kg/m ²)	24.3 \pm 3.1	24.6 \pm 3.4	0.48
Serum IgE (mean \pm SD, IU/mL)	1,250 \pm 450	1,200 \pm 420	0.31

The sociodemographic characteristics of the patients in both groups were comparable, as shown in **Table I**. There were no statistically significant differences between Group A (Corticosteroids Only) and Group B (Corticosteroids + Itraconazole) in terms of age (34.5 \pm 8.2 vs. 33.8 \pm 7.9 years, $p = 0.56$), gender distribution (male/female: 32/47 vs. 28/47, $p = 0.62$), BMI (24.3 \pm 3.1 vs. 24.6 \pm 3.4 kg/m², $p = 0.48$), serum IgE levels (1,250 \pm 450 vs. 1,200 \pm 420 IU/mL, $p = 0.31$), and Lund-Mackay scores (18.5 \pm 3.2 vs. 18.8 \pm 3.0, $p = 0.45$). This suggests that baseline characteristics were well-matched across the two study groups.

Table II highlights the recurrence rates of allergic fungal rhinosinusitis (AFRS) post-surgery. The recurrence rate was significantly lower in Group B, with only 10.0% ($n = 05$) of patients experiencing recurrence compared to 25.5% ($n = 12$) in Group A ($p = 0.004$). This suggests that the addition of itraconazole to corticosteroid therapy may be effective in reducing recurrence rates.

Post-surgical symptom improvement and quality of life outcomes, as presented in **Table III**, showed a statistically significant advantage in Group B. Patients receiving combination therapy demonstrated greater reductions in SNOT-22 scores (mean reduction: 20 vs. 12 points, $p < 0.001$), indicating better symptomatic relief. Similarly, RSDI scores improved more substantially in Group B (mean improvement: 25 vs. 15 points, $p < 0.001$), suggesting a greater enhancement in disease-specific quality of life.

VARIABLE	GROUP A (CORTICOSTEROIDS ONLY)	GROUP B (CORTICOSTEROIDS + ITRACONAZOLE)	P-VALUE
Lund-Mackay Score (mean ± SD)	18.5 ± 3.2	18.8 ± 3.0	0.45

Table II: The recurrence rates of allergic fungal rhinosinusitis (AFRS) post-surgery (n=47 in each group)

GROUP	Frequency	Percentage	P-VALUE
Group A (Corticosteroids Only)	12	25.5%	0.004
Group B (Corticosteroids + Itraconazole)	05	10.6%	

$$\chi^2 = 8.32, p = 0.004.$$

Table III: Symptom Improvement and Quality of Lifemetrics post-surgery

OUTCOME MEASURE	GROUP A (CORTICOSTEROIDS ONLY)	GROUP B (CORTICOSTEROIDS + ITRACONAZOLE)	P-VALUE
SNOT-22 Scores (Mean Reduction)	12 points (baseline: 45)	20 points (baseline: 44)	< 0.001
RSDI Scores (Mean Improvement)	15 points (baseline: 60)	25 points (baseline: 59)	< 0.001

Discussion

The present study demonstrates that the addition of itraconazole to corticosteroid therapy significantly reduces the recurrence rates of allergic fungal rhinosinusitis (AFRS) following endoscopic sinus surgery (ESS). Specifically, Group B (Corticosteroids + Itraconazole) exhibited a recurrence rate of 10.0%, markedly lower than the 25.5% observed in Group A (Corticosteroids Only), with a statistically significant difference ($p = 0.004$). These findings align with previous research indicating the efficacy of itraconazole in managing AFRS which reported that itraconazole, when used as primary medical management, improved treatment outcomes in AFRS patients.^{14,15,16}

In terms of symptom relief and quality of life, patients receiving combination therapy (Group B) experienced greater improvements. The mean reduction in SNOT-22 scores was 20 points in Group B, compared to 12 points in Group A ($p < 0.001$), indicating superior symptomatic relief. Similarly, the RSDI scores improved by 25 points in Group B versus 15 points in Group A ($p < 0.001$), suggesting a more substantial

enhancement in disease-specific quality of life. These outcomes are consistent with findings from other studies that have highlighted the benefits of combining antifungal agents with corticosteroids. Previous studies reported that systemic corticosteroids, when used postoperatively, significantly increased the time to revision surgery in AFRS patients.^{17,18}

The comparable sociodemographic characteristics between the two groups, including age, gender distribution, BMI, serum IgE levels, and Lund-Mackay scores, suggest that the observed differences in outcomes are attributable to the treatment modalities rather than baseline disparities. This strengthens the argument for the adjunctive use of itraconazole in the postoperative management of AFRS.^{19,20}

While the study provides compelling evidence supporting the combination therapy, it is essential to consider potential limitations. The sample size, though adequate, may benefit from expansion in future studies to enhance generalizability. Additionally, the duration of follow-up was limited to 12 months; longer follow-up periods could provide

more insight into the long-term efficacy and safety of itraconazole use.

The adjunctive use of itraconazole with corticosteroids post-ESS appears to be a promising strategy in reducing recurrence rates and improving symptomatology and quality of life in AFRS patients.

Conclusion

The addition of itraconazole to corticosteroid therapy significantly reduced the recurrence rates of AFRS and led to greater symptomatic relief and improved quality of life post-surgery. These findings support the adjunctive use of itraconazole in postoperative AFRS management to enhance long-term outcomes.

References

- Rojita M, Samal S, Pradhan P, Venkatachalam VJJoc, JCDR dr. Comparison of steroid and itraconazole for prevention of recurrence in allergic fungal rhinosinusitis: a randomized controlled trial. 2017;11(4):MC01.
- Salil A, Joy N, Faizal BJCO. A prospective study comparing itraconazole alone versus systemic steroids alone as adjuncts to topical steroids in the post-operative management of allergic fungal rhinosinusitis. 2023;48(2):356-62.
- Reda R, Wageh W, Fawaz M, Mikhael WJTEJoO. Comparison between local steroids and local steroids plus itraconazole effect in prevention of recurrence of allergic fungal sinusitis in hypertensive and/or diabetic patients. 2019;35:25-9.
- Shah B, Kajal S, Bhalla A, Madan K, Viswanathan G, Thakar A, et al. Prolonged Itraconazole Therapy as Sole Treatment for Patients with Allergic Fungal Rhinosinusitis. 2024;134(2):545-51.
- Patro SK, Verma RK, Panda NK, Chakrabarti A, Singh PJAJoR, Allergy. Efficacy of preoperative itraconazole in allergic fungal rhinosinusitis. 2015;29(4):299-304.
- Salil A, Joy N, Faizal B. A prospective study comparing Itraconazole and systemic steroids as an adjunct to topical steroids in the post-operative management of Allergic fungal rhinosinusitis. Authorea Preprints. 2022 Jun 2.
- Mostafa BE, Fadel M, Mohammed MA, Hamdi TA, Askoura AM. Omalizumab versus intranasal steroids in the post-operative management of patients with allergic fungal rhinosinusitis. *European Archives of Oto-Rhino-Laryngology*. 2020 Jan;277:121-8.
- Medikeri G, Javer A. Optimal management of allergic fungal rhinosinusitis. *Journal of Asthma and Allergy*. 2020 Sep 11:323-32.
- Thanasumpun T, Batra PS. Oral antifungal therapy for chronic rhinosinusitis and its subtypes: a systematic review. In *International Forum of Allergy & Rhinology* 2011 Sep (Vol. 1, No. 5, pp. 382-389). Hoboken: Wiley Subscription Services, Inc., A Wiley Company.
- Mahfouz El-Ghadafi AY, Tantawy AZ, Elnashar I, Said A. The Role of Systemic Itraconazole in Management of Allergic Fungal Rhinosinusitis. *Zagazig University Medical Journal*. 2022 Nov 1;28(6.2):66-73.
- Ponikau JU, Sherris DA, Kephart GM, Kern EB, Congdon DJ, Winn DM, et al. Features of allergic fungal sinusitis and its relation to eosinophilic mucin rhinosinusitis. *J Allergy Clin Immunol*. 2005;115(2):370-6.
- Ebbens FA, Georgalas C, Fokkens WJ. The efficacy of antifungal therapy in allergic fungal rhinosinusitis: a randomized, double-blind, placebo-controlled trial. *J Allergy Clin Immunol*. 2006;118(3):725-32.
- Venekamp RP, Thompson MJ, Hayward G, et al. Systemic and topical antifungal treatment for chronic rhinosinusitis. *Cochrane Database Syst Rev*. 2014;(1):CD008263.
- El-Sayed Tantawy AZ, El-Nashar IS, Said Mohamed AR, Mahfouz El-Ghadafi AY. The Role of Systemic Itraconazole in Management of Allergic Fungal Rhinosinusitis. *Zagazig University Medical Journal*. 2022 Nov 3;28.
- Hashemi M, Fereidani A, Berjis N, Okhovat SA, Eshaghain A. Effectiveness of itraconazole on clinical symptoms and radiologic findings in patients with recurrent chronic rhinosinusitis and nasal polyposis. *Advanced Biomedical Research*. 2014 Jan 1;3(1):162.

Chua AJ, Jafar A, Luong AU. Update on allergic fungal rhinosinusitis. *Annals of Allergy, Asthma & Immunology*. 2023 Sep 1;131(3):300-6.

Mamatha KR, Sankar RG, Varghese GT, Puttamadaiah G, Suhas K. A study to assess the efficacy of oral itraconazole as an add-on to steroids in allergic fungal rhinosinusitis in a tertiary care hospital. *National Journal of Physiology, Pharmacy and Pharmacology*. 2024 Aug 1;14(8):1598.

Afzal M, Baloch MO, Nadeem MA. Efficacy of Post-Operative Oral Prednisolone for the Control of Disease in Allergic Fungal Sinusitis. *Journal of Sheikh Zayed Medical College (JSZMC)*. 2021 Jun 30;12(02):18-.

Ferguson BJ. What role do systemic corticosteroids, immunotherapy, and antifungal drugs play in the therapy of allergic fungal rhinosinusitis?. *Archives of Otolaryngology-Head & Neck Surgery*. 1998 Oct 1;124(10):1174-8.

Masterson L, Egro FM, Bewick J, Erskine SE, Clark A, Javer AR, Philpott CM. Quality-of-life outcomes after sinus surgery in allergic fungal rhinosinusitis versus nonfungal chronic rhinosinusitis. *American Journal of Rhinology & Allergy*. 2016 Mar;30(2):e30-5.

