

AFRS Pathophysiology

Aggregate Grade of Evidence: B (Level 2: 7 studies; level 4: 30 studies; Table X-30).

X.E.2 | AFRS Management

As a subtype of CRSwNP, there are significant similarities in the management of AFRS and CRSwNP. Several reviews on the management of AFRS often advocate the primary role of sinus surgery to remove fungal laden eosinophilic mucin and extended courses of postoperative oral corticosteroids in AFRS.^{1693,1714,1731} Despite the widespread acceptance of these treatment modalities, there are no studies that have specifically addressed surgery as the recommended initial step in the management of AFRS as compared to medical therapy or the optimal duration of postoperative oral corticosteroids.

X.E.2.a. AFRS Management: Anti-Fungal Therapy (Oral and Topical)

Although several clinical trials have addressed the role of oral antifungals in CRS, only a handful of studies have specifically included AFRS. Consequently, ICAR-RS-2016 concluded that there were insufficient studies to either recommend for or against the use of antifungals in AFRS. Since then, 4 additional studies in this area have been published.

Patro et al.¹⁷³² performed a prospective randomized study on 52 AFRS patients to either 4 weeks of preoperative itraconazole or not. Both groups experienced a significant improvement in SNOT-20 and Lund-Mackay scores at 24 weeks postoperatively.

Rojita et al.,¹⁷³³ in a prospective trial of 60 patients with AFRS undergoing ESS, compared the postoperative use of topical nasal steroids to itraconazole (100 mg BID) for 6 months. Hepatic enzyme abnormalities occurred in 6.6% of patients while taking itraconazole. Both groups experienced a significant decrease in SNOT scores, IgE levels and similar recurrence rates.

Verma et al.¹⁷³² performed an unblinded RCT on 175 patients examining the use of itraconazole (100 mg BID) given either pre- or post-operatively. All patients received 6 weeks post-operative oral steroid taper. SNOT-20, LM and endoscopy scores improved with itraconazole as compared to oral steroids alone; with better scores in the preoperative itraconazole group.

Finally, a Cochrane systematic review¹⁷³⁴ examining topical and oral antifungals in AFRS patients was unable to make a recommendation due to the low quality of evidence.

Overall, there continues to be few studies examining oral or topical antifungal therapy for AFRS and most are either low-level, have few subjects, and/or contain methodologic weaknesses. At this point, there is insufficient evidence to recommend for or against antifungal therapy in AFRS.

Antifungal Therapy for AFRS

Aggregate Grade of Evidence: C (Level 1: 1 study; level 2: 2 studies; level 3: 3 studies; level 4: 5 studies; Table X-31).

Benefit: May decrease time to recurrence and improve endoscopic scores.

Harm: Potential elevation in liver enzymes associated with medication side effect. Some antifungals are metabolized by the CYP system and can affect steroid metabolism.

Cost: Low.

Benefits-Harm Assessment: Benefit appears modest at best.

Value Judgments: Itraconazole appears to only mildly improve the recurrence and postoperative symptoms of AFRS with potential risk of adverse events.

Policy Level: Option.

Intervention: Can consider topical or oral antifungals in AFRS patients recalcitrant to maximal topical steroid therapy and immunotherapy.

X.E.2.b. AFRS Management: Immunotherapy

Type I hypersensitivity to fungi is a criterion for AFRS diagnosis and may represent a significant component of the pathophysiology of AFRS; however no new study has been published since ICAR-RS-2016. As such, Gan et al. remains the only evidence-based review with recommendations regarding IT for AFRS.¹¹⁰¹ They identified 2 level 3b studies and 3 level 4 studies which showed some value in treating AFRS with IT. Unfortunately, there were significant drawbacks in all of the studies including small sample sizes, mixture of IT with other medical treatments, and the absence of standardized control groups. Given the limited current evidence, additional clinical trials are needed to examine this question.