Efficacy of Different Modalities in Treatment of Different Types of Fungal Sinusitis

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ABSTRACT

Background: Fungal rhinosinusitis (FRS) includes a spectrum of disease processes that vary in clinical presentation, histologic appearances, and treatment options.

Objective: This systematic review was done to reach the effective and safe method in management of FRS.

Patients and Methods: Meta-analysis was performed in accordance to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). This study used the published articles (from Jan1985 to Jan2018) in treatment of FRS via search in several databases.

Results: Finally, forty-five studies were included in this study. Fifteen of them assessed the treatment of fungal ball (FB) using mainly the functional endoscopic sinus surgery (FESS) the success rate was 98.1%. Twenty included studies have evaluated the management of allergic fungal sinusitis (AFS) via FESS, Systemic steroids, Antifungals and immunotherapy. The results showed that FESS represents the first-line, followed by aggressive medical therapies, the recurrence rate after postoperative steroids was 20.6%, postoperative antifungals was 40% and after immunotherapy was 9.1%. Ten included studies considered the Invasive Fungal sinusitis. The results showed that the combination of systematic antifungal therapy and aggressive surgical debridement was the treatment of the choice.

Conclusion: FESS is the treatment of choice for FB. AFS treatment consists of surgical extirpation of the allergic mucin and followed by anti-fungal therapy, Immunotherapy, and corticosteroids. Treatment of invasive fungal sinusitis includes surgical resection of necrotic tissues, systemic antifungal therapy and reversal of immune dysfunction.

Key Words: Allergic fungal rhinosinusitis, antifungal in AFS, aspergillus in FB, fungus ball rhinosinusitis, immunotherapy in AFS, invasive fungal rhinosinusitis.

INTRODUCTION

The first step in treatment for any AFS patient is paranasal sinus surgery to both remove all obstructing inspissated allergic mucin and resect all diseased hypertrophic sinus mucosa. Failure to adequately surgically remove all sinus disease leads to higher AFS relapse rates[1]. The addition of postoperative oral corticosteroids (OCS) in AFS play an important role to reduces overall disease activity, including decreasing both symptoms and surgical recurrence rates[2]. The aim of management of fungal ball is to remove the allergic mucin and good aeration of the sinuses. The treatment of IFS requires reversal of the underlying predisposing condition, surgical debridement and appropriate systemic antifungal therapy[3].

AIM OF THE WORK:

A systematic review of effective and safe method in management of different types of fungal sinusitis either by medical or surgical approaches or even combined.

PATIENTS AND METHODS:

We performed this systematic review and meta-analysis in accordance to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analyses Of Observational Studies in Epidemiology (MOOSE) statements. PRISMA and MOOSE are reporting checklists for Authors, Editors, and Reviewers of Meta-analyses of interventional and observational studies. According to International Committee of Medical Journal association (ICMJE), reviewers must report their findings according to each of the items listed in those checklists.

Study Selection and Eligibility Criteria:

The present review included studies that fulfilled the following criteria: Studies that included patients with different types of fungal rhinosinusitis whether it was invasive or non-invasive. Studies that assessed the efficacy and safety of different surgical and medical modalities
for the management of fungal rhinosinusitis Studies that compared those modalities with none or any comparison; Studies that reported any of the following outcomes: success rates, recurrence rates, and the incidence of complications. Studies that were either prospective or retrospective studies.

**Search Strategy and Screening**: Studies include published medical articles (from Jan1985 to Jan 2018) concerning the comparison between Different modalities for treatment of different types of fungal sinusitis through searching different databases such as Medline and PubMed using the following keywords in different combinations (treatment of fungal sinusitis) and (treatment of invasive fungal sinusitis) and (treatment of non invasive fungal sinusitis) and (Antifungal therapy for chronic rhinosinusitis) and (Immunotherapy in the treatment of allergic fungal sinusitis) and (role of surgical debridment in invasive fungal rhinosinusitis). Articles will be screened to fulfill the following criteria, restricted to English language, applied on humans.

**Screening**: Retrieved citations were imported into End Note X7 for duplicates removal. Subsequently, unique citations were imported into an Excel sheet and screened by two independent reviewers; the screening was conducted in two steps: title and abstract screening, followed by a full-texts screening of potentially eligible records.

**Article inclusion criteria**: Treatment of different types of fungal sinusitis. Published in English language (from Jan1985 to Jan 2018). Conducted on human subjects.

**Article exclusion criteria**: Published in other languages “not in English”. Conducted on animals. Review articles and case reports.

**Data Extraction**: Data entry and processing were carried out using a standardized Excel sheet and reviewers extracted the data from the included studies. The extracted data included the following domains: (1) Summary characteristics of the included studies; (2) Baseline characteristics of studied populations; and (3) Study outcomes. All reviewers’ independently extracted data from the included articles and any discrepancies were solved by discussion.

**Dealing with Missing Data**: Missing standard deviation (SD) of mean change from baseline was calculated from standard error or 95% confidence interval (CI) according to Altman49.

**Data Synthesis**: Continuous outcomes were pooled as mean difference (MD) or standardized mean difference (SMD) using inverse variance method, and dichotomous outcomes will be pooled as relative risk (RR) using Mantel-Haenszel method. The random-effects method was used under the assumption of existing significant clinical and methodological heterogeneity. We performed all statistical analyses using Review Manager (RevMan) 5.3 or Open Meta-analyst for windows.

**Assessment of Heterogeneity**: We assessed heterogeneity by visual inspection of the forest plots, chi-square, and I-square tests. According to the recommendations of Cochrane Handbook of Systematic Reviews and meta-analysis, chi-square p-value less than 0.1 denote significant heterogeneity while The I-squared is interpreted as follows: 0% to 40%: unimportant heterogeneity. 30% to 60%: moderate heterogeneity. 50% to 90%: substantial heterogeneity. 75% to 100%: considerable heterogeneity.

**RESULTS:**

A. **Fungal Ball**: Fifteen included studies (No. = 856 patients) assessed different modalities for the management of fungal ball infection. The majority of the included studies were retrospective studies, while only one study was prospective cohort. The sample size of the included studies ranged from 25 to 160 patients and the duration of follow up ranged from 12 months to 93 months. The success rate of FESS ranged from 91% to 100%. (Table 1). In terms of success rates of FESS, 9 studies reported the success rates. The overall effect estimate showed that FESS led to success rate of 98.1% (95% CI 96.6 – 99.6%). (Figure 1).

B. **Allergic Fungal Sinusitis**: (Table 2) showed twenty included studies (No=806 patients) that have assessed the efficacy and safety of different modalities for the management of allergic fungal sinusitis via FESS, Post-FESS Systemic steroids, Antifungals and immunotherapy. The results showed that FESS represents the first-line management strategy of AFS, followed by aggressive medical therapies, the recurrence rate after postoperative steroids was 20.6-% (95% CI 5.5 – 35.7%). (Figure 2). The incidence of recurrence was higher with postoperative antifungals was 40%. (Figure 3). While, after immunotherapy was 9.1% (95% CI 1.6 – 16.5%). (Figure 4).

C. **Invasive Fungal Sinusitis**: Ten studies (No=327 patients) recruited patients with Invasive Fungal Sinusitis. All included studies were retrospective studies with a sample size ranged from 11 to 90 patients. Most of the patients had hematological diseases with an age ranged from 34 to 82 years old. (Table 3). The results showed that combination of systematic antifungal therapy and aggressive surgical debridement are the treatment of choice. In addition, the reported mortality rates ranged from 18 to 60%. The overall effect estimate showed that the mortality rates of acute fungal sinusitis was 23.1% (95% CI 12.6 – 33.7%). (Figure 5).
Table 1: Summary Characteristics of the included studies which assessed the treatment of fungal ball

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study Design</th>
<th>Country</th>
<th>No</th>
<th>Age</th>
<th>Affected Sinus</th>
<th>Positive culture</th>
<th>Treatment Modality</th>
<th>Approaches</th>
<th>Follow-up (months)</th>
<th>Success Rate</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eloy et al.[5]</td>
<td>2004</td>
<td>Retrospective Study</td>
<td>Belgium</td>
<td>66</td>
<td>NA</td>
<td>Maxillary and sphenoid sinus</td>
<td>Aspergillus fumigatus</td>
<td>surgery (mainly endonasal approach)</td>
<td>Middle antrostomy or sphenoidotomy; inferior antrostomy; a limited approach through the canine fossa.</td>
<td>NA</td>
<td>91%</td>
<td>10%</td>
</tr>
<tr>
<td>Montone et al.[6]</td>
<td>2012</td>
<td>Retrospective Study</td>
<td>USA</td>
<td>161</td>
<td>(18–90)</td>
<td>Maxillary sinus and sphenoid/ethmoid sinuses</td>
<td>Aspergillus sp. (66%)</td>
<td>surgery (mainly endonasal approach)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Pagella et al.[7]</td>
<td>2007</td>
<td>Retrospective Study</td>
<td>Italy</td>
<td>81</td>
<td>(19–90)</td>
<td>Maxillary sinus and sphenoid/ethmoid sinuses</td>
<td>Aspergillus sp. (34%)</td>
<td>Functional endoscopic sinus</td>
<td>Ethmoidectomy; Meatoectomy; sinusoscopy via fossa canina was associated; trans-nasal sphenoidotomy; transethmoidal approach.</td>
<td>NA</td>
<td>95%</td>
<td>5%</td>
</tr>
<tr>
<td>Pagella et al.[8]</td>
<td>2009</td>
<td>Retrospective Study</td>
<td>Italy</td>
<td>33</td>
<td>NA</td>
<td>Maxillary sinus</td>
<td>Aspergillus sp. (34%)</td>
<td>Functional endoscopic sinus</td>
<td>Canine fossa approach.</td>
<td>93</td>
<td>95.4%</td>
<td>NA</td>
</tr>
<tr>
<td>Chobillon[9]</td>
<td>2004</td>
<td>Retrospective Study</td>
<td>France</td>
<td>9</td>
<td>NA</td>
<td>Maxillary sinus</td>
<td>Aspergillus sp. (100%)</td>
<td>Functional endoscopic sinus</td>
<td>Canine fossa approach.</td>
<td>93</td>
<td>100%</td>
<td>0</td>
</tr>
<tr>
<td>Suresh et al.[10]</td>
<td>2016</td>
<td>Prospective study</td>
<td>USA</td>
<td>14</td>
<td>(11–90)</td>
<td>Maxillary sinus and sphenoid/ethmoid sinuses</td>
<td>Aspergillus sp. (34%)</td>
<td>Functional endoscopic sinus</td>
<td>NA</td>
<td>12</td>
<td>100%</td>
<td>3%</td>
</tr>
<tr>
<td>Klossek et al.[11]</td>
<td>1997</td>
<td>Retrospective Study</td>
<td>France</td>
<td>109</td>
<td>(20-86)</td>
<td>Maxillary sinus and sphenoid/ethmoid sinuses</td>
<td>Aspergillus sp. (56%)</td>
<td>Functional endoscopic sinus</td>
<td>Middle antrostomy; combination of middle and inferior antrostomies; simple sphenoidotomies</td>
<td>29</td>
<td>96%</td>
<td>4%</td>
</tr>
<tr>
<td>Nicolai et al.[12]</td>
<td>2009</td>
<td>Retrospective Study</td>
<td>Italy</td>
<td>160</td>
<td>(19-85)</td>
<td>Maxillary sinus and sphenoid/ethmoid sinuses</td>
<td>NA</td>
<td>Functional endoscopic sinus</td>
<td>Middle antrostomy or sphenoidotomy; inferior antrostomy; a limited approach through the canine fossa.</td>
<td>24</td>
<td>100%</td>
<td>1%</td>
</tr>
<tr>
<td>Lee et al.[13]</td>
<td>2007</td>
<td>Retrospective Study</td>
<td>Korea</td>
<td>86</td>
<td>(20-79)</td>
<td>Maxillary sinus and sphenoid/ethmoid sinuses</td>
<td>Aspergillus sp. (72%)</td>
<td>Functional endoscopic sinus</td>
<td>Middle antrostomy or sphenoidotomy; inferior antrostomy; a limited approach through the canine fossa.</td>
<td>100%</td>
<td>0.6%</td>
<td></td>
</tr>
</tbody>
</table>
Table 2: Summary Characteristics of the included studies which assessed the treatment of AFR.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study Design</th>
<th>Country</th>
<th>Sample Size</th>
<th>Age</th>
<th>Treatment Modality</th>
<th>Follow-up (months)</th>
<th>Success Rate</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Champagne et al.</td>
<td>2010</td>
<td>Prospective study</td>
<td>Taiwan</td>
<td>48</td>
<td>32 (12 - 68)</td>
<td>Endoscopic sinus surgery</td>
<td>12</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Verma et al.</td>
<td>2013</td>
<td>Prospective study</td>
<td>India</td>
<td>40</td>
<td>27.8 (10-65)</td>
<td>Endoscopic sinus surgery</td>
<td>32</td>
<td>90%</td>
<td>NA</td>
</tr>
<tr>
<td>Masterson et al.</td>
<td>2016</td>
<td>Retrospective</td>
<td>USA</td>
<td>2</td>
<td>51 ±14</td>
<td>Endoscopic sinus surgery</td>
<td>12</td>
<td>100%</td>
<td>NA</td>
</tr>
<tr>
<td>Kupferberg et al.</td>
<td>1997</td>
<td>Retrospective</td>
<td>USA</td>
<td>26</td>
<td>NA</td>
<td>Oral steroids</td>
<td>14.5</td>
<td>92%</td>
<td>37.5%</td>
</tr>
</tbody>
</table>

Fig. 1: Success rate of FESS in fungal ball.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Study Design</th>
<th>Country</th>
<th>Age (Range)</th>
<th>Treatment</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kuhn and Javer</td>
<td>2000</td>
<td>Retrospective study</td>
<td>USA</td>
<td>11</td>
<td>Oral steroids</td>
<td>27</td>
<td>NA 18.2%</td>
</tr>
<tr>
<td>Woodworth et al.</td>
<td>2004</td>
<td>Prospective cohort study</td>
<td>USA</td>
<td>21</td>
<td>Prednisolone 1 mg/kg for 10 days preoperatively</td>
<td>NA</td>
<td>NA 5.6%</td>
</tr>
<tr>
<td>Landsberg et al.</td>
<td>2007</td>
<td>Prospective cohort study</td>
<td>Israel</td>
<td>8 23 (14 -38)</td>
<td>Systemic steroid treatment</td>
<td>NA</td>
<td>NA 5.6%</td>
</tr>
<tr>
<td>Rojita et al.</td>
<td>2007</td>
<td>Retrospective study</td>
<td>India</td>
<td>24</td>
<td>Topical steroids</td>
<td>6</td>
<td>100% 23.5%</td>
</tr>
<tr>
<td>Gupta et al.</td>
<td>2007</td>
<td>Prospective cohort study</td>
<td>Israel</td>
<td>8 31.1</td>
<td>Topical steroids</td>
<td>6</td>
<td>100% 23.5%</td>
</tr>
<tr>
<td>Kupferberg et al.</td>
<td>1997</td>
<td>Retrospective study</td>
<td>USA</td>
<td>26</td>
<td>Oral antifungals alone</td>
<td>14.5</td>
<td>NA 79.2%</td>
</tr>
<tr>
<td>Rains and Mineck</td>
<td>2003</td>
<td>Retrospective study</td>
<td>USA</td>
<td>139</td>
<td>Oral antifungals</td>
<td>NA 31.4</td>
<td>50.4%</td>
</tr>
<tr>
<td>Seiberling and Wormald</td>
<td>2009</td>
<td>Retrospective study</td>
<td>Australia</td>
<td>23 49 (23 -60)</td>
<td>Oral antifungals</td>
<td>15.7</td>
<td>NA 13%</td>
</tr>
<tr>
<td>Rojita et al.</td>
<td>2017</td>
<td>Prospective cohort study</td>
<td>USA</td>
<td>30 5 (560)</td>
<td>Oral antifungals</td>
<td>6</td>
<td>NA 31.2%</td>
</tr>
<tr>
<td>Khalil et al.</td>
<td>2011</td>
<td>Randomized Controlled Trial</td>
<td>Egypt</td>
<td>50 35.4 (18 - 61)</td>
<td>Topical antifungals</td>
<td>9</td>
<td>100% 11.8%</td>
</tr>
<tr>
<td>Jen et al.</td>
<td>2004</td>
<td>Prospective cohort study</td>
<td>USA</td>
<td>16 39 (59 -74)</td>
<td>Topical antifungals</td>
<td>3</td>
<td>NA 25%</td>
</tr>
<tr>
<td>Folker et al.</td>
<td>1998</td>
<td>Retrospective study</td>
<td>USA</td>
<td>11 39 (19 –72)</td>
<td>IT with fungal and nonfungal antigens, corticosteroids, antibiotics</td>
<td>30</td>
<td>NA NA</td>
</tr>
<tr>
<td>Mabry et al.</td>
<td>1997</td>
<td>Prospective cohort study</td>
<td>USA</td>
<td>9</td>
<td>IT given weekly basis based on sensitivities to fungal and antifungal antigens up to 12 months</td>
<td>8.5</td>
<td>NA 5%</td>
</tr>
<tr>
<td>Mabry and Mabry</td>
<td>1997</td>
<td>Prospective cohort study</td>
<td>USA</td>
<td>10</td>
<td>IT given initially weekly for a year then extended to biweekly basis</td>
<td>NA</td>
<td>NA 10%</td>
</tr>
<tr>
<td>Bassichis et al.</td>
<td>2001</td>
<td>Prospective cohort study</td>
<td>USA</td>
<td>60 42.7 (7 -75)</td>
<td>IT given for relevant antifungal and fungal antigens</td>
<td>12</td>
<td>NA 11%</td>
</tr>
<tr>
<td>Greenhaw et al.</td>
<td>2011</td>
<td>Prospective cohort study</td>
<td>USA</td>
<td>14 36.6 (12.8)</td>
<td>IT given for relevant antifungal and fungal antigens</td>
<td>NA</td>
<td>NA 0%</td>
</tr>
</tbody>
</table>
**Table 3:** Summary Characteristics of the included studies which assessed the treatment of invasive fungal sinusitis.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study Design</th>
<th>Country</th>
<th>Population</th>
<th>Sample Size</th>
<th>Age</th>
<th>Treatment Modality</th>
<th>Mortality rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen et al. [33]</td>
<td>2011</td>
<td>Retrospective study</td>
<td>Taiwan</td>
<td>patients with 3 hematological disease</td>
<td>46</td>
<td>NA</td>
<td>antifungal combination therapy and/or aggressive surgical debridement</td>
<td>41%</td>
</tr>
<tr>
<td>Saedi et al. [34]</td>
<td>2011</td>
<td>Retrospective study</td>
<td>Iran</td>
<td>Patients with infection limited to the nose and sinuses were selected</td>
<td>30</td>
<td>49±19.3</td>
<td>antifungal combination therapy and aggressive surgical debridement</td>
<td>60%</td>
</tr>
</tbody>
</table>
Among causes of sinonasal inflammatory disease, fungal sinusitis is a relatively uncommon but well-established clinical entity. Fungi are ubiquitous in the environment, and can colonize the upper respiratory tract mucosa when fungal spores are inhaled. In people with normal immune function, the fungal growth is kept in check. With impaired host immunity, fungi can invade host mucosa and cause invasive disease. Fungal sinusitis consists of a heterogeneous group of disorders, with diversity in the affected patient population, mechanism of disease, clinical presentation, histopathology, imaging appearances, treatment, and overall prognosis.

Fungal ball is one of the most common form of noninvasive fungal sinusitis that is usually preceded saprophytic fungal infestation. The fungal ball is characterized by an extramucosal, entangled mass of fungi usually associated with minimal mucosal inflammation. In the present systematic review and meta-analysis, 15 included studies (No = 856 patients) assessed the efficacy and safety of different antifungal combination therapy and/or aggressive surgical debridement.
modalities for the management of non-invasive fungal ball infection with a sample size ranged from 9 to 160 patients and the duration of follow up ranged from 12 months to 93 months.

The current body of evidence shows that fungal balls are more common in middle-age or older women, while maxillary sinus is the most commonly involved sinus. In line with our findings, Nicolai and colleagues performed a retrospective study that included 160 patients with fungal ball of the paranasal sinuses who underwent endoscopic surgery. They found that the majority of patients were females; in addition, the maxillary sinus was the most commonly involved (84%), followed by the sphenoid sinus (14%) and, rarely, the ethmoid or frontal sinus.

On the other hand, surgical opening of the natural sinus ostium with evacuation of fungal debris is the treatment of choice. After removal of fungal hyphae, the sinus mucosa generally returns to a normal state of health and no additional treatment is usually necessary. In the present systematic review, all of the included studies utilized functional endoscopic sinus surgery for the management of fungal ball. Our analysis showed that that functional endoscopic sinus surgery led to success rate of 98.1% (95% CI 96.6 – 99.6%) and recurrence rate of 2.3% (95% CI 0.8 – 3.8%). Moreover, the reported perioperative complication and recurrence rates were very low among the included studies.

In terms of the surgical approaches, the removal of maxillary sinus fungal ball may be long and difficult, in particular when the anterior and/or inferior recesses are involved, as they are notoriously more difficult to manage with the classic endoscopic technique. Therefore, some authors have advocated a combination of the pure endoscopic technique and a complementary endoscopic canine-fossa approach, using a trocar in the canine fossa (the so-called “double approach”) so as to arrive at a complete resection of the fungus ball.

Nevertheless, canine fossa approach may make fungal ball surgery in the long. This leads to an increase in the surgical procedure time, a higher risk of complications due to the difficulty of the technique and, consequently, a higher cost. Consequently, numerous authors have proposed various techniques without intervening on the canine fossa. Chao and Liu in 2006 proposed the so-called “gauze technique.” The merits of this technique do not only lie in its simplicity and the high learning curve but also include a higher speed of execution and lower costs than the technique without gauze, as the materials used are part of the standard supplies in any operating theatre.

Moreover, this atraumatic technique has potentially no complications other than those related to the classic endoscopic technique. In order to avoid recurrence, there are two cornerstones, to widen the maxillary sinus ostium as much as possible and to take care of pushing the gauze very gently so as to preserve the periosteum of the maxillary sinus; even if the mucosa is injured, it will heal as long as the periosteum is intact.

In the present systematic review and meta-analysis, two included studies assessed the “gauze technique” to clean out the fungal ball from the sinus without resorting to any destructive procedures. The earlier study by Chao et al. reported that neither recurrence nor complication was noted among 15 adults with FB of the maxillary sinus.

More recently, Garofalo and colleagues performed a retrospective, cross-sectional, and descriptive study of 25 patients affected by maxillary fungus ball: 19 were treated by the “gauze technique” and 6 were treated without “gauze technique”. The authors reported a success rate of 96% (24/25 patients) with the gauze technique.

In the present review, 20 included studies (No. = 608 patients) assessed the efficacy and safety of different modalities for the management of allergic fungal sinusitis.

Surgical therapy represents the first-line management strategy of AFRS. Most clinical series describe surgical therapy to remove polyps, open sinus ostia, and clear eosinophilic fungal mucin, followed by aggressive medical therapies. From the literature, it appears that surgery in combination with other medical treatments leads to improved outcomes.

In the present systematic review, a wide range of post-surgical medical therapies were investigated by the included studies. The efficacy of systemic steroids has been studied in 6 included studies with a sample size ranged from 8 to 30 patients (oral steroids = 2 studies; and systemic steroids = 3 studies). The included studies agreed that postoperative steroids significantly reduce postoperative mucosal disease, improve symptoms by endoscopic grading, and reduce inflammatory markers. In addition, two study assessed the efficacy of topical steroid in form of low-volume metered-dose steroid spray (0.25 mg/2 mL or 0.5 mg/2 mL in 240 mL saline or higher concentration). The results of the meta-analysis showed that the recurrence rates after postoperative steroids was 20.6-% (95% CI 5.5 – 35.7%). Moreover, the post-surgical steroids improved the Sino-nasal Outcome Test (SNOT-20) by 24.09% (95% CI 11.52 – 36.6%).
On the other hand, limited evidence reported benefits of oral antifungal therapies in patients with AFRS. In the present systematic review and meta-analysis, the use of systemic antifungal therapy in patients with AFR has been studied in four studies. Itraconazole at 200 mg to 400 mg PO daily in divided doses were used with an average duration of follow-up ranging from 6-15.7 months. Oral antifungals were reported to lead a significant reduction in symptoms, reduction in dependence on oral steroids and prevention of disease recurrence. While, two included studies explored the use of topical antifungals in the management of AFS patients. The antifungal regimens included fluconazole nasal spray irrigation with a fluconazole solution through the nasal fossa. The results of the present meta-analysis showed that the recurrence rates after postoperative antifungals was 40% (95% CI 17.8 – 62.2%); while the rate of symptoms improvement after postoperative antifungals was 57.7% (95% CI 33 – 82.5%).

Finally, Rains and colleagues conducted a retrospective chart review in 139 patients with AFRS and cited findings using their protocol including high dose itraconazole, low-dose oral steroids, and topical corticosteroids. The authors reported a 50.3% recurrence rate, with 20.5% of those patients requiring reoperation. They concluded that their regimen, with its use of itraconazole, was safe.

AFRS is defined by a Type 1 hypersensitivity to fungus, so it stands to reason that immunotherapy (IT) could feasibly blunt the immune response to fungus and decrease disease burden. Allergen IT was used to treat allergic fungal sinusitis in five included studies in the present systematic review. Those studies supported that indicates IT may be beneficial in AFRS patients. However, all studies used IT in conjunction with other medical therapies. Despite case-control studies, none of the comparison groups were placed on the same medical regimen to decipher the true effect of IT. The results of the meta-analysis showed that the recurrence rates after immunotherapy was 9.1% (95% CI 1.6 – 16.5%).

Gan and colleagues conducted a systematic review of the available literature regarding IT in AFRS. This review identified and assessed 6 medical modalities for AFRS in the literature: oral steroids; topical steroids; oral antifungals; topical antifungals; immunotherapy; and leukotriene modulators. The results showed that IT potentially reduces mucosal inflammation and the amount of topical/systemic corticosteroids required.

Treatment of invasive fungal sinusitis includes surgical resection of necrotic tissues, systemic antifungal antibiotics, and reversal of immune dysfunction. The goal of surgical therapy is to remove necrotic tissue. The treatment employed in all studies was a combination of systematic antifungal therapy and aggressive surgical debridement. The included studies use a variety of topical and intravenous antifungals including (amphotericin B plus capsosfugin and amphotericin B plus voriconazole or amphotericin B alone. The results of the meta-analysis showed that mortality rate of acute fungal sinusitis was 23.1% (95% CI 12.6 – 33.7%).

CONCLUSION

Our meta-analysis assessed different modalities for management of fungal ball, via classic endoscopic technique, Canine-fossa approach, gauze technique and osteoplastic approach for FB of the maxillary sinus. The results showed that functional endoscopic sinus surgery led to success rate of 98.1%.

Allergic fungal sinusitis treatment consists of surgical extirpation of the allergic mucin and polyps with maintenance of adequate sinus drainage followed by medical therapy consists of topical intranasal steroids nasal irrigations, anti fungal therapy Immunotherapy, and systemic corticosteroids. The use of Post-ESS Steroids significantly reduces postoperative mucosal disease, improves symptoms by endoscopic grading, and reduces inflammatory markers. The use of systemic antifungal therapy in patients with AFR has been reported to lead to a significant reduction in symptoms and a reduction too in dependence on oral steroids, but recurrence rate is higher than steroids. However, possible harms may include renal failure, elevated liver enzymes, rash, headache, malaise and fatigue. Treatment of invasive fungal sinusitis includes surgical resection of necrotic tissues, systemic antifungal therapy, and reversal of immune dysfunction. The mortality rates of invasive fungal sinusitis was 23.1%.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES


TREATMENT OF FUNGAL SINUSITIS


