Are systemic corticosteroids effective in the treatment of allergic fungal sinusitis ?

(Systematic review)

For partial fulfillment of master degree in Otorhinolaryngology.

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(بسم الله الرحمن الرحيم)

الرَّحْمَنُ (١) عَلَّمَ الْقُرْآنَ (٢) خَلَقَ الإِنسَانَ (٣) عَلَّمَهُ الْبَيَانَ (٤) الشَّمْسُ وَالْقَمَرُ بِحُسْبَانٍ (٥) وَالنَّجْمُ وَالشَّجَرُ يَسْجُدَانِ (٦) وَالسَّمَاءَ رَفَعَهَا وَوَضَعَ الْمِيزَانَ (٧) أَلاَّ تَطْغَوْا فِي الْمِيزَانِ (٨)

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Introduction

Allergic fungal sinusitis is a relatively newly characterized disease entity that commands a great deal of interest. Large amounts of information are being generated addressing the underlying etiology of the disease, its clinical presentation, and forms of treatment **(Marple, 2006).**

Allergic fungal sinusitis was first described in the early 1980s by Millar et al (1981) in the United Kingdom and by Katzenstein et al (1983) in the United States. The organisms responsible for most cases of this disease are *Aspergillus* sp. and members of the family of dematiaceous fungi. Typically, patients are young and immunocompetent, and they present with a history of atopic disease **(Ikram et al, 2009).**

Although controversy still exists, recent evidence supports the theory that allergic fungal sinusitis represents an immunologic, rather than infectious disease process. An improved understanding of this underlying disease process has led to an evolution in its treatment **(Ikram et al, 2009).**

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 **(Ikram et al, 2009).**

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 **(Ikram et al, 2009).**

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. 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 **(Ikram et al, 2009).**

Aim of the work

Our study will be a systematic review to evaluate if systemic corticosteroids are effective in the treatment of allergic fungal sinusitis or not?

This objective will be achieved by the following steps:

1- Determination of the target subject.

2- Identification and location of articles.

3- Screening and evaluation of articles.

4- Data collection.

5- Data analysis.

6- Reporting and interpreting (results).

7- Discussion and conclusions.

Definition:

Allergic fungal sinusitis is a disease of the nose and paranasal sinuses, characterized by immune hypersensitivity reaction to fungal antigens that produces allergic mucin, which accumulates within paranasal sinuses **(Ikram et al, 2008).**

The role of fungus in chronic rhinosinusitis:

While the overall impact that fungus plays a role in the etiology and pathogenesis of chronic inflammatory rhinosinusitis may be argued, there is little disagreement that fungus does play some role in selected cases **(Marple, 2006).**

The currently recognized forms of fungal diseases of the paranasal sinuses can be broadly classified as either invasive or non-invasive. Invasive forms of fungal rhinosinusitis, including indolent, fulminant, and granulomatous variants, are fortunately rare and confined to relatively well-defined groups of patients who are frequently immunocompromised. In such cases, failure to appropriately identify and treat the disease can potentially lead to death or disfigurement **(Marple, 2006).**

In contrast to the danger posed by invasive forms of fungal disease, in some cases fungi appear to have the ability to incite

varying degrees of chronic inflammatory sinonasal disease. The degree to which non-invasive fungi impact local inflammation may vary according to the disease **(Marple, 2006).**

Fungal balls (previously referred to as mycetoma) are recognized as self-limited collections of matted fungal hyphae confined most commonly to the maxillary sinus, and while they may be locally destructive, they represent the mildest trigger of regional inflammation **(Marple, 2006).**

At the opposite end of the inflammatory spectrum, under certain circumstances small amounts of fungal exposure appear to have the ability to stimulate a relatively robust regional reaction. One example of this is that of allergic rhinitis caused by exposure to fungal allergens **(Marple, 2006).**

While the concept of allergy to fungus is not new, the potential for fungus to serve as a non-invasive stimulus of mucosal inflammation was realized with the recognition of allergic fungal rhinosinusitis over two decades ago **(Marple et al, 2002).**

In fact allergic fungal sinusitis was first recognized in the late 1970s by pulmonologists and pathologists who noted the

distinct clinical and immunologic similarities that it shared with allergic bronchopulmonary aspergillosis **(Katzenstein et al, 1983; Marple, 2006).**

As general awareness of allergic fungal rhinosinusitis has grown, an increasing amount of literatures has followed describing its clinical appearance, immunologic characteristics, incidence, geographic distribution, and response to various forms of therapy. Despite the differing designs and conclusions of each of these studies, all share one important feature: patients who were selected for study were identified based upon the clinical manifestations of their disease **(Marple, 2006).**

Associated fungi:

Early reports, which implied that Aspergillus species was the primary causative fungus associated with allergic fungal sinusitis, were based largely upon the morphologic appearance of the fungal hyphae identified histologically, as well as the recognized clinical and immunologic similarities shared between allergic fungal sinusitis and allergic bronchopulmonary aspergillosis. This notion was further supported by early serologic testing, published by Katzenstein, demonstrating elevated specific IgE to Aspergillus flavus in two patients afflicted with allergic fungal sinusitis **(Katzenstein et al, 1983).**

As the availability of culture-specific allergic fungal sinusitis information increased, however, it became apparent that many fungal species could be associated with development of the disease **(Cody et al, 1994).**

In a 1996 review of the English literature performed by Manning, a total of 263 cases of allergic fungal sinusitis were identified, of which 168 cases (64%) yielded positive fungal cultures. Of those 168 positive cultures, 87% were dematiaceous genera while only 13% yielded Aspergillus **(Manning and Holman, 1998)**.

Although not typically associated with invasive forms of fungal disease, dematiaceous fungi are recognized for the role they play in inhalant allergy. Specific genera within the dematiaceous family include Bipolaris, Curvularia, Exserohilum, Alternaria, Drechslera, Helminthosporium and Fusarium **(Marple, 2006).**

Immunopathology of Allergic Fungal Sinusitis:

Much of what we know about the immunopathogenesis of allergic fungal sinusitis draws a strong analogy to allergic bronchopulmonary aspergillosis. In allergic bronchopulmonary aspergillosis, Aspergillus fumigatus is found within inspissated

bronchial allergic mucin in a patient with severe asthma; very high titres of fungal-specific IgG and IgE are found in serum along with peripheral eosinophilia (**Greenberger et al, 1986; Marple, 2006).**

In Bipolaris spicifera allergic fungal sinusitis, Bipolaris spicifera is found within inspissated sinus allergic mucin in a patient with hypertrophic sinus disease; high titres of fungal-specific IgG are found in serum, but not as high as in allergic bronchopulmonary aspergillosis **(Schubert and Goetz, 1998)**.

Although such patients are uniformly skin test positive for type I immediate hypersensitivity to Bipolaris spicifera, fungal-specific IgE in serum is not higher than that found in common Bipolaris spicifera inhalant atopy **(Schubert and Goetz, 1998).**

As in allergic bronchopulmonary aspergillosis, the vast majority of patients with allergic fungal sinusitis are allergic to multiple aeroallergens, with a 100% incidence of inhalant atopy reported in patients with allergic fungal sinusitis from the southwest of the United States **(Schubert and Goetz, 1998)**.

Total serum IgE levels are often elevated in allergic fungal sinusitis, but not as high as in allergic bronchopulmonary

aspergillosis. Peripheral eosinophilia does not occur uniformly in allergic fungal sinusitis, and erythrocyte sedimentation rates are generally not elevated **(Schubert and Goetz, 1998)**.

Allergic fungal sinusitis has even occasionally been seen concomitantly with the analogous bronchial disorder, usually involving the same fungal organism in both the upper (sinonasal) and lower (bronchial) airways, with the suggested term being sinobronchial allergic mycosis syndrome **(Venarske and deShazo, 2002)**.

Taken together, the Immunopathology of allergic fungal sinusitis and allergic bronchopulmonary aspergillosis appears similar but not identical, suggesting a magnified immunological response in allergic bronchopulmonary aspergillosis as compared with allergic fungal sinusitis. The reason(s) for this are unknown, but may relate to target organ and/or aetiological microbial differences between the two disorders **(Schubert, 2004).**

Although the exact pathogenesis of allergic fungal sinusitis remains unknown, it has been characterized as similar to the pathogenesis of allergic bronchopulmonary aspergillosis **(Manning et al, 1993; Manning and Holman, 1998; Ferguson**