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The Effect of the Oral Itraconazole on the Management of Allergic Fungal Sinusitis

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ABSTRACT

Allergic fungal rhinosinusitis (AFS) is the most common form of fungal sinus disease. Its recurrence rate is high despite numerous strategies to prevent it. Oral itraconazole is an antifungal agent that seems to be benefit to the patients with AFS. Because management of allergic fungal sinusitis after surgery is difficult and prolonged steroid use has significant side effects and there are a group of patients who are unresponsive to standard treatment. So this study was designed to compare the outcome of AFS after addition of oral itraconazol to the treatment protocol. This Prospective randomized controlled clinical study done on 57 patients who were diagnosed with AFS by clinical, radiologic, histopathologic, and laboratory workup and who subsequently underwent Functional Endoscopic Sinus Surgery (FESS). Postoperatively, these patients were randomized into two treatment groups matched for sex, age, and socioeconomic status. Systemic and topical nasal steroids with(group A) or without (group B)oral itraconazole(100 mg b.i.d) for at least 2 months was used postoperatively. 7 patients didn't follow up their treatment so 25 cases of group A continued to follow up. The data obtained were analyzed statistically using descriptive Statistics and report results base on tables and figures. 11 patients of group A had endoscopic and radiological improvement and this improvement was maintained during the follow up period, while 5 had radiologic evidence of recurrence of sinus within 6 months, 7 patients had recurring polyp in one or both sides and two patients had to stop treatment after two months due to abnormal liver function tests. Mean pretreatment IgE was 876 microgram/L and posttreatmentIgE was 754 microgram/L. 16 patients (64%) of group B (control group) had recurring polyp in one or both sides, while 3 (12%) had radiologic evidence of recurrence of sinus and nasal polyps within 6 months, 6 patients had endoscopic and radiological improvement and this improvement was maintained during the follow up period. Mean follow up time was 12.4 months. Oral Itraconazole may be of benefit as an adjunct in the management of refractory AFS. It may prolong the time of recurrence. But Steroids continue to remain the mainstay of treatment and more research is needed to define the role of systemic antifungal drugs.

Key words: Oral Itraconazole, Allergic Fungal Sinusitis, Steroid, FESS.

INTRODUCTION

The allergic fungal sinusitis (AFS) cycle suggests that atopy, continuous antigenic exposure, and inflammation all have key roles in the perpetuation of the disease. Over the past 2 decades, AFS has become increasingly prevalent. It is now believed to be an allergic reaction to aerosolized environmental fungi, usually of the dematiaceous species in an immunocompetent host[1,2]. Most patients with AFS have history of allergic rhinosinusitis, approximately 5-10% of patients affected by chronic rhinosinusitis actually carry a diagnosis of allergic fungal sinusitis (AFS).

The incidence of AFS appears to be impacted by geographic factors. Review of the world's literature reveals the majority of sites reporting cases of AFS to be located in temperate regions with relatively high humidity[3]. On the basis of a postulated schema of the pathophysiology of AFS, a variety of treatment plans addressing its multiple contributing factors has emerged[4,5]. Medical control of the disease has made use of various combinations of antifungal medications, corticosteroids, and immunotherapy, with varying degrees of disease control. Attempts to control this disease by only partially addressing the underlying causes likely have contributed to a high rate of recidivism[6,9]. Successful treatment of AFS requires that the treatment plan account for each factor responsible for the propagation of the disease. In theory, individually accounting for each of these factors provides for the best chance of long-term disease control. This comprehensive approach to management depends on complete removal of all fungal mucin (usually requiring surgery) and long-term prevention of recurrence through either immunomodulation (immunotherapy and/or corticosteroids) or fungistatic antimicrobials. There are various issues relating to the use of concomitant medical therapy in the treatment of Allergic Fungal sinusitis. Firstly, there are different forms of fungal sinusitis, and each requires a specific therapeutic regimen, targeted at the pathogen. Secondly, there are numerous toxicity related issues which need to still be addressed. Thirdly, many newer antifungal drugs are extremely expensive. Lastly and most importantly, there are few randomized controlled trials which able to valid a various studies[7,8,11]. This study was designed to compare the outcome of AFS after addition of oral itraconazole to the treatment protocol.

MATERIALS AND METHODS

This Prospective randomized controlled clinical study done on 57 patients with clinically diagnosed (AFS), they were treated with FESS followed by postoperative systemic and topical nasal steroids with or without oral itraconazole(100 mg b.i.d) for at least 2 months. It was conducted at Imam University Hospital from March 2010 to June 2013. All patients were evaluated with pre- and post-treatment endoscopic examinations, serum IgE and questionnaires of quality of life(Snot 20). Monthly liver function tests were done to monitor for hepatic side effects of itraconazole. All Patients were diagnosed as AFS based on a modification of the Bent and Kuhn criteria.(1. Nasal polyposis,2. Characteristic computed tomographic scan features, 3.Allergic mucin on histologic examination or characteristic appearance on endoscopic examination, 4. Raised total serum immunoglobulin E.)

The nature of the procedure was explained to the patients and An Informed consent, with an emphasis on the possibility of hepatic affection secondary to chemical hepatitis, was obtained from all patients. The data obtained were analyzed statistically using the SPSS 18.

RESULT

Base on Tables1,2,3,4 and 5 and Figures1 and 2 that consist of results for case and control groups: 11 patients of group A had endoscopic and radiological improvement and this improvement was maintained during the follow up period, while 5 had radiologic evidence of recurrence of sinus within 6 months, 7 patients had recurring polyp in one or both sides and two patients had to stop treatment after two months due to abnormal liver function tests.

16 patients (64%) of group B (control group) had recurring polyp in one or both sides , while 3 (12%) had radiologic evidence of recurrence of sinus and nasal polyps within 6 months, 6

Table 1:Descriptive Statistics for case and control groups

	Groups	N	Minimum	Maximum	Mean	Std. Deviation
Age	Case(A)	25	12	56	30.32	11.037
	Control(B)	25	14	45	29.96	9.572

Table 2: Frequency and percent base on sex in case and control groups

	Frequency (case group)	Frequency (control group)	Percent (case group)	Percent (control group)
Female	17	16	68	64
Male	8	9	32	36
Total	25	25	100	100

Table 3: Sides of suffering in case and control groups

	Frequency (case group)	Frequency (control group)	Percent (case group)	Percent (control group)
Bilateral	19	14	76	56
Unilateral	6	11	24	44
Total	25	25	100	100

Table 4: Case and control groups Complications

	Frequency (case group)	Frequency (control group)	Percent (case group)	Percent (control group)
No complication	23	25	92	100
Yes(elevation of liver enzymes)	2	0	8	0
Total	25	25	100	100

Table 5: Follow up results for case and control groups

	Frequency (case group)	Frequency (control group)	Percent (case group)	Percent (control group)
no evidence or recurrence	11	6	44	24
recurring polyp in one or both sides	7	16	28	64
radiological evidence of recurrence	5	3	20	12
don't complete the follow up period	2	0	8	0
Total	25	25	100	100

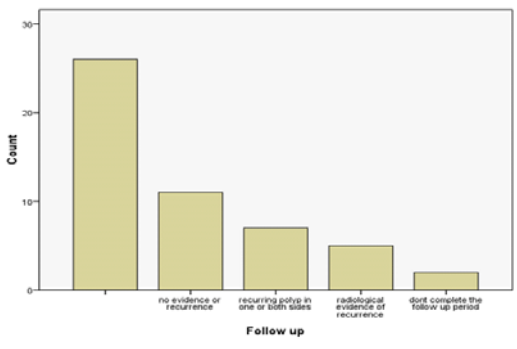

Fig. 1: Follow up results for case group

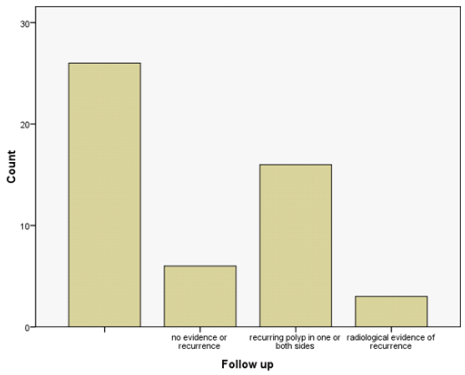

Fig. 2: Follow up results for control group

patients had endoscopic and radiological improvement and this improvement was maintained during the follow up period.

DISCUSSION

Allergic fungal sinusitis (AFS) has a variety of treatment plan. One of the new plan is using Itraconazole as an adjunct therapy of AFRS. However, more studies, including a prospective randomized clinical trial, are required to determine if itraconazole is an effective method or not. Successful treatment of AFS requires arranging the treatment plan account for each factor that responsible for the propagation of this disease. Because of potent anti-inflammatory and immunomodulatory effects of corticosteroids it is suitable to control the recurrence. But the optimal dosing regimen and length of therapy remain unclear[4,10]. Follow up of AFS patients show high recurrence despite of corticosteroid using in these patients. So another method of AFStherapy is Systemic antifungal therapy is suggested. Antifungal therapy often was used in an attempt to provide some degree of control over recurrence of AFS.

Denning et al. studied the effect of systemic itraconazole in patients with ABPA and demonstrated a decrease in total IgE[10]. He used itraconazole in a 6 patients and found that they were able to decrease the amount of prednisone required to prevent disease relapse and progression. Rains and Mineckreported using up to 400 mg of itraconazole daily and then tapering down to 200 mg a day over 3 months without any major side effects, they reported only a 4% prevalence of elevated liver enzymes. Itraconazole appears to have a modest benefit as an adjunct in the management of refractory AFS[12]. Ferguson points out that the expense, limited available data, and potential drug-related morbidity of systemic antifungal therapy may limit the usefulness of this form of treatment for noninvasive fungal disease[13]. Itraconazole and fluconazole offer a slightly safer form of antifungal therapy but still may give rise to drug-induced cardiac dysrhythmias, hepatic dysfunction, urticaria, and anaphylaxis. According to our study we propose that prolonged antifungal therapy should be instituted in patients with AFS to achieve good results regarding the rate of recurrence.

CONCLUSIONS

Oralltraconazole may be of benefit as an adjunct in the management of refractory AFS. It may prolong the time of recurrence. But Steroids continue to remain the mainstay of treatment and more research is needed to define the role of systemic antifungal drugs. Itraconazole appears to have a modest benefit as an adjunct in the management of refractory AFS.

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