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Efficacy of Post-Operative Oral Prednisolone for the Control of Disease in Allergic Fungal Sinusitis

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Abstract

Background: Ambiguity persists regarding the dosage, frequency, and duration for the use of oral steroids in Allergic Fungal Sinusitis (AFS).

Objective: To assess the efficacy of post-operative oral steroid (prednisolone) for the control of disease in Allergic Fungal Sinusitis.

Methodology: This was a comparative study, conducted at Bahawal Victoria Hospital, Bahawalpur from January 2019 to March 2019. A total of 40 patients, aged 18 or above with weight over 50 kilograms, having proved Allergic Fungal Sinusitis (AFS) as per criteria defined by Deshazo and Swain, were recruited for this study. All the patients were enrolled within 14 days of excisive sinus surgery adopting endoscopic sinus surgery with or without open methods. Group A (n=20) received oral steroids while Group B (n=20) received a placebo. Patients of both groups also used fluticasone nasal spray and oral itraconazole. Evaluation of all the patients was done at the time of enrollment, 6 and 12 weeks. Data were analyzed by SPSS version 21.

Results: Out of a total of 40 patients, there were 17 (42.5%) male. After 6 weeks of continuous therapy in both the study groups, 14 (70%) patients of Group A showed complete relief of symptoms in comparison to none in Group B (p-value = 0.001). After 12 weeks of therapy having tapering off in both study groups, all patients in Group A had complete relief of symptoms in comparison to only one (5%) in Group B (p-value = 0.001).

Conclusion: Oral steroids of prednisolone, along with inhaled steroids therapy for a minimum of 12 weeks after excisive sinus surgery were found efficacious for the control of disease in patients with Allergic Fungal Sinusitis.

Keywords: Allergic Fungal Sinusitis, Sinus surgery, Prednisolone, Symptoms

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Introduction

Allergic fungal sinusitis (AFS) was 1st explained towards the end of the last century.[1,2] It was characterized by atopy, sinonasal polyposis, and the existence of allergic mucin. The pathophysiology of AFS includes type 1 and type 3 hypersensitivity reactions to various fungi, mainly aspergillus species and dematiaceous fungi.[3]

AFS has been increasingly observed in some parts of the United States,[4] Sudan,[5] India,[6] and Saudi Arabia.[7] In a local study from Pakistan, it was seen that an increasing trend was noted regarding the incidence of ASF from the Northern regions of Pakistan.[8] In that same local study, nasal obstruction and nasal discharge were the commonest complaints in patients having AFS whereas nasal polyps on anterior rhinoscopy were mainly found in ASF.[8] Lot of work has been done in the last couple of decades exploring AFS, but still, many concerns exist with regards to its diagnosis and treatment. Surgical debridement of involved sinuses adopting endoscopic sinus surgery or open methods for removal of all allergic mucin aiming drainage is considered to be the main option of treatment.[9] Quite a few agents have been experimented with in the perioperative span to minimize the rates of recurrence of AFS. Oral steroids, inhaled steroids, oral antifungals as well as topical antifungals are some of the most common adoption options. Some researchers also recorded superior outcomes adding systemic steroids, oral antifungals, topical antifungals, and immunotherapy.[10-12] In almost all of the studies conducted, inhaled steroids have been part of therapy all around the world.

The ambiguity of the data findings exists regarding the use of oral steroids in AFS for prevention of recurrence or to decrease the need for repeated

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surgeries as there are limited numbers of trials available to demonstrated better results of oral steroids to other forms of therapies. Ambiguity also persists regarding the dosage, frequency, and duration of the use of oral steroids in AFS. So, we planned this comparative study to note the efficacy of post-operative oral steroids (prednisolone) for the control of disease in Allergic Fungal Sinusitis.

Methodology

This was a comparative study, conducted at Bahawal Victoria Hospital Bahawalpur from January 2019 to March 2019. A total of 40 patients, aged 18 or above with weight over 50 kilograms, having proved AFS as per criteria defined by Deshazo and Swain[13] were recruited for this study. All the patients were enrolled within 14 days of excisive sinus surgery adopting endoscopic sinus surgery with or without open methods. Patients having histological proof of tissue invasion, or who had immunodeficiencies were excluded. Patients who had indications that made oral steroids contraindicated (like active tuberculosis, uncontrolled hypertension) were also not enrolled. Numbered paper slips were employed for patient randomization to 2 groups. Group A (n=20) received oral steroids while Group B (n=20) received a placebo. Both surgeons and patients were blinded from the form of treatment adopted in this study. Approval from institutional research and the ethical committee was taken for this study. Informed consent was also sought from all the study participants.

All study data were recorded on a predesigned proforma. Demographical details along with data about the extent of the disease as well surgical procedures performed on both groups were noted. Patients in Group A were administered oral steroid therapy, which was oral prednisolone (50mg once a day for a duration of 6 weeks). The dose was tapered over an additional period of 6 weeks.[11] Group B used a placebo adopting the same schedule. Patients of both groups were using oral ranitidine at a dose of 150 mg once a day as well as fluticasone nasal spray (2 puffs once a day). Oral itraconazole (200 mg once a day for 3 months) was also given to all the patients of both groups.

Evaluation of all the patients was done at the time of enrollment, 6 and 12 weeks. At the time of enrollment, patients were enquired about symptoms related to AFS. At 6 and 12 weeks after the enrollment, patients of both groups were assessed for all the symptoms that were enquired preoperatively. Relief of symptoms was noted in terms of complete, partial, or no relief in all the patients.

Objective assessment was also made at 6 and 12 weeks after the surgery adopting a standard endoscopic staging system described by Kupferberg SB et al as stage 0 (No evidence of disease), stage 1 (Mucosal edema ± allergic mucin), stage 2 (Polyploidal mucosa ± allergic mucin) or stage 3 (Polypoidal mucosa with allergic mucin).[14]

Material that resembled allergic mucin on endoscopy was sent for histopathological examination and fungal culture. Likewise, polyps (if present) were sent seeking histopathological examination. Separate specimens were dispatched aiming at fungal culture as well as histopathology. At 6 weeks point, if evaluation of any individual revealed stage 2 or worse, that individual was to be eliminated from this trial and surgery was to be considered.

Fasting plasma glucose, postprandial plasma glucose, serum calcium levels, blood pressure, eye examination as well as clinical evaluation seeking side effects of steroid treatment were made.

SPSS version 21.0 was used for data entry and statistical analysis. Both study groups were compared with regards to symptoms relief and endoscopy score at 6 and 12 weeks points utilizing the chi-square test. An independent sample t-test was used to compare the means for age and symptoms duration between the groups taking p-value ≤ 0.05 as significant.

Results

Out of a total of 40 patients, there were 17 (42.5%) male and 23 (57.5%) female. Overall mean age was found to be 38±11.5 years. Overall, the mean duration of symptoms was noted to be 31.15±24.6 months, ranging from 1 month to 9 years. Amongst all patients, nasal obstruction was the commonest symptom noted in 39 (97.5%), followed by sneezing in 33 (82.5%) and nasal discharge in 31 (77.5%). At baseline, demographic data along with symptoms and sinus involvement amongst patients of both groups did not show any statistically significant difference as shown by Table-I. Direct microscopy for fungal elements revealed a positive culture in all

of the patients. Tissue erosion was not evident in any of the cases.

After 6 weeks of continuous therapy in both the study groups, 14 (70%) patients of Group A showed complete relief of symptoms in comparison to none in Group B (p-value = 0.001). At the same point of time, assessment adopting rigid nasal endoscopy revealed that 14 (70%) of the patients of Group A achieved Stage 0, whereas only one (5%) patient in Group B was Stage 0, while all others in Group B were Stage 1 or above (p-value = 0.001).

After 12 weeks of therapy having tapering off in both study groups, all patients in Group A, had complete relief of symptoms in comparison to 2 (10.0%) in Group B (p-value = 0.001). (Table-II)

All 20 patients in Group A were having transient weight gain whereas 7 (35%) developed cushingoid features involving the face and the neck. Side effects experienced in the 1st 6 weeks of treatment were subsided following tapering off in all the patients of Group A. Table-III shows endoscopic staging at 6 and 12 weeks in both groups.

Table-I: Baseline Characteristics of Patients

Characteristics	Group A (n=20)	Group B (n=20)	Total	P value
Gender				
Male	7 (35%)	10 (50%)	17 (42.5%)	0.337
Female	13 (65%)	10 (10%)	23 (57.5%)	
Age in Years (Mean ±SD)	37.70±11.3	38.55±12	38.13±11.5	0.0819
Symptoms in months(Mean ±SD)	29.8±24	32.5±25.8	31.15±24.6	0.734
Symptoms				
Nasal Congestion	19 (95%)	20 (100%)	39 (97.5%)	0.311
Nasal Discharge	16 (80%)	15 (75%)	31 (77.5%)	0.705
Sneezing	17 (85%)	16 (80%)	33 (82.5	0.677
Facial Pain	1 (5%)	2 (10%)	3 (7.5%)	0.548
Headache	4 (20%)	3 (15%)	7 (17.5%)	0.677
Proptosis	12 (60%)	10 (50%)	22 (55.5%)	0.525
Sinuses Involved				
Maxillary	19 (95%)	20 (100%)	39 (97.5%)	0.311
Ethmoid	20 (100%)	20 (100%)	40 (100%)	
Sphenoid	20 (100%)	19 (95%)	39 (97.5%0	0.311
Frontal	17 (85%)	16 (80%)	33 (82.5%)	0.677
Multisinus Involvement				
Unilateral Disease	5 (25%)	6 (30%)	11 (27.5%)	0.723
Bilateral Disease	15 (75%)	14 (70%)	29 (72.5%)	

Table-II: Relief of Preoperative Symptoms at 6 and 12 Weeks in Both Groups

Relief of Symptoms	Group-A (n=20)	Group-B (n=20)	Total	P-value
6 Weeks				
Complete Relief	14 (70%)	0 (0%)	14 (35%)	0.001
Partial or No Relief	6 (30%)	20 (100%)	26 (65%)	
12 Weeks				
Complete Relief	20 (100%)	2 (10%)	22 (55%)	0.001
Partial or No Relief	0 (0%)	18 (90%)	18 (45%)	

Table-III: Endoscopic Staging at 6 and 12 weeks in Both Groups

Endoscopic Staging	Group A (n=20)	Group B (n=20)	Total	P value
6 Weeks				
Stage 0	14 (70%)	1 (5%)	15 (37.5%)	0.001
Stage 1 or above	6 (30%)	19 (95%)	25 (62.5%)	
12 Weeks				
Stage 0	20 (100%)	2 (10%)	22 (55%)	0.001
Stage 1 or above	0 (0%)	18 (90%)	18 (45%)	

Discussion

Adequate sinus surgery is considered to be a globally endorsed way and 1st line treatment for patients of AFS.[9,13,14] Following surgery, oral and topical corticosteroids have been shown to produce an excellent response in terms of relief from symptoms. Katzenstein AA et al studied steroid therapy in of the earliest findings evaluating the efficacy of steroids in AFS. The authors found useful outcomes and suggested that a more in-depth review regarding the role of steroid therapy in patient's AFS needs to be done in prospective trials.[2] Waxman JE and Coworkers[15] suggested that steroids should be started immediately in the postoperative period following full surgical extirpation of the disease. A study done by Kinsella A[16] showed that all those cases who had oral steroids for 2 to 4 weeks postoperatively had no recurrence at 6 months follow up. DeShazo RD and Swain RE[13] also suggested oral steroids in the postoperative period following surgery in AFS cases.

In a study from India, Rupa V ET al[11] evaluated 24 patients diagnosed with AFS and who underwent sinus surgery. It was observed that 66.6% of patients who were receiving oral prednisolone after 6 weeks of treatment had complete relief of symptoms while at the end of 12 weeks of treatment, all the patients had complete relief of preoperative symptoms (p-value < 0.001). The researchers in that study concluded that postoperative prednisolone for a minimum of 12 weeks is recommended in all those cases that undergo excisive surgery for AFS.[11]

A difference exists regarding the dosage of prednisolone. Most authors have suggested oral prednisolone at a dose of 0.5mg per kilogram per day for 2 weeks which is followed by alternate day therapy for a further 3 to 6 months.[15, 17] Allphin AL et al[17] recommended that topical steroids can be administered for a longer duration of time following tapering off of oral steroid for the achievement of disease-free state. Others have endorsed oral prednisolone as 40mg per day for 4 days, 30 mg per day for 4 days, and 20mg per day for 1 month.[14] the dosage was asked to be fined tuned at a minimum possible dose where the patient can maintain stage 0 states. It has also been observed that dosage <15mg per day on every alternate day turned out to have a recurrence, pointing towards longer maintenance of steroid therapy.[14] In the current work, we employed prednisolone at a dosage of 50mg per day for 6 weeks that was aimed at rapid minimization of inflammatory edema of sinus mucosa while also promoting better drainage of operated sinuses. After 6 weeks of continuous therapy in both the study groups, 14 (70%) patients of Group A showed complete relief of symptoms in comparison to none

in Group B (p-value = 0.001). At the same point of time, assessment adopting rigid nasal endoscopy revealed that 14 (70%) of the patients of Group A achieved Stage 0, whereas only one (5%) patient in Group B was Stage 0, while all others in Group B were Stage 1 or above (p-value = 0.001). After 12 weeks of therapy having tapering off in both study groups, all patients in Group A had complete relief of symptoms in comparison to 2 (10.0%) in Group B (p-value < 0.001). Studies in the past have also recommended continuous steroid therapy for up to 1 year for best clinical outcomes whereas longer maintenance with oral steroids has shown prevention in recurrence.[18]

Conclusion

Oral steroid along with inhaled steroids therapy for a minimum of 12 weeks after excisive sinus surgery was found efficacious for the control of disease in patients with Allergic Fungal Sinusitis.

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