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Low Dose, Short-Term Oral Methylprednisolone for Nasal Polyps: A Randomized Double-Blind Placebo-Controlled Trial

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ABSTRACT

Objectives: To determine the efficacy of a 7-day treatment of methylprednisolone 16mg in reducing the size of nasal polyps and on improvement of nasal symptoms.

Methods:

Design: Randomized double-blind placebo-controlled trial
Setting: Out-patient department of the East Avenue Medical Center
Patients: Patients 18 years old and above with nasal polyposis determined by history and endoscopic examination

Results: There was a significant decrease in polyp size by an average of 16% ($P < .05$) among 12 out of the 23 patients (52.17 %) in the steroid group versus placebo. The treatment group also exhibited an improvement in nasal symptoms of rhinorrhea, congestion and anosmia compared to the placebo.

Conclusion: Medical treatment with oral methylprednisolone given at a low dose of 16 mg for one week resulted in reduction of the size of nasal polyps and improved the symptoms of rhinorrhea, nasal congestion and anosmia. Other associated symptoms like headache, epistaxis, sneezing, itchiness, epiphora, cough, postnasal drip, throat discomfort, facial pain, eye complaints and fever did not differ between the steroid and placebo groups.

Recommendation: One week of oral steroids can be used to treat nasal polyps initially. If there is response, this mode of management can be combined with a long-term course of intranasal steroid sprays[9,10]. Patients who do not respond may be referred for surgery.

Keywords: *Nasal polyposis, methylprednisolone, rhinorrhea, nasal congestion, anosmia*

NASAL polyposis is a condition resulting from chronic inflammation of the nasal and paranasal sinus mucosa, leading to a projection of benign edematous masses from the meatus to the nasal cavity. Multiple factors interact to initiate the surge of inflammatory responses that culminate in polypoid nasal growth[1]. Altered sinonasal functions lead to a variety of symptoms like nasal stuffiness and obstruction, anterior and posterior rhinorrhea, loss of the sense of smell, and facial pain. These make it the most incapacitating illness of the nasal cavity and paranasal sinuses[2].

Corticosteroids are the mainstay in the medical management of nasal polyps. Systemic corticosteroids are considered the most effective pharmacological agents as they dramatically decrease mucosal inflammation and suppress the immune response against environmental

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Table 1. Dose of oral steroids as recommended by different authors

Corticosteroid	Recommended dose	Author
Dexamethasone	12 mg tapered to 3 mg within 9 days	Lund, 1995[13]
Methylprednisolone	64 mg tapered to 10 mg within 11 days	Rasp, 2000 [14]
	1mg/kg/day tapered to ¼ of the dose within 16 days	Tuncer, 2003 [9]
Prednisolone	60 mg tapered to 5 mg within 16 days	van Camp, 1994 [6]
	1mg/kg/day for 5 days	Bonfils, 2003 [10]
	1mg/kg/day for 10 days	Slavin, 1995 [16]
Fluocortolone	560 mg oral tapered for 12 days or 715 mg tapered for 20 days	Damm, 1999 [5]

Table 2. Four-point grading scale for polyps (McKay and Lund)

Grade 0	no polyps
Grade I	small polyps not reaching the edge of the lower edge of the middle turbinate
Grade II	medium-sized polyps extending between the upper and lower edges of the inferior turbinate
Grade III	large polyps extending below the lower edge of the inferior turbinate

Table 3. Subjective Clinical Scoring System
Symptom score: 0 = absent; 1 = mildest; 10 = worst

1	Headache	8	Cough
2	Epistaxis	9	Post-nasal drip
3	Rhinorrhea	10	Throat discomfort
4	Congestion	11	Facial pain
5	Sneezing	12	Eye complaints
6	Itchiness	13	Fever
7	Epiphora	14	Anosmia

Table 4. Score Scale System

Grade	Score Scale
0	0
I	1 – 10
II	11 – 20
III	21 - 30

irritants and bacterial/fungal antigens[3]. They can reach all parts of the nose and sinuses, including the olfactory cleft and middle meatus, and can better improve the sense of smell, in contrast to intranasal topical steroids[4].

Woodworth[3] demonstrated a significant decrease (radiographically and endoscopically) in extent of nasal polyps and an improvement of nasal symptom scores with systemic corticosteroids. Other studies of oral steroids reported success rates of 50 and 72%[5,6], but these were non-randomized.

Most randomized control trials involving the use of topical intranasal steroids reported overall success rates between 60.9 to 80%[7,8]. Other studies combining a short-term course of oral steroids and a long-term course of intranasal steroids showed a reduction of polyp volume in 85 to 88% of patients with concomitant improvement in nasal symptoms[9,10].

The main concerns with the use of systemic corticosteroids are adverse effects that can occur after prolonged use. Patients given daily doses of 100mg hydrocortisone (or the equivalent 20 mg amount of synthetic steroid methylprednisolone) for longer than 2 weeks may undergo "Iatrogenic Cushing's Syndrome[11]". Other serious adverse effects include peptic ulcers and their consequences, hypomania or acute psychoses, sodium and fluid retention and loss of potassium[11]. In the management of nasal polyps, oral corticosteroids are given as a short-term course of 5-10 days with or without tapering[12] or a long-term course of 12-21 days with tapering[3,5,6,9] (Table 1).

This study aims to assess the efficacy of low-dose systemic corticosteroids given for 7 days in the treatment of nasal polyps.

MATERIALS AND METHODS

The study was conducted at the East Avenue Medical Center from August 2004 to September 2005. Of an initial 113 patients, 48 patients met the inclusion criteria: (1) age 18 years or older and (2) presence of nasal polyps on endoscopic examination. Excluded were patients with: (1) co-morbidities like diabetes mellitus, hypertension, acid peptic disease/gastritis, psychosis: (2) purulent sinonasal discharge; (3) use of rhinitis or asthma medications; (4) hypersensitivity to corticosteroids. Informed consent was obtained for the study.

The 48 patients were randomized equally into steroid and placebo groups using computer-generated numbers. The steroid group was treated with methylprednisolone, 16 mg once a day after breakfast for 7 days. Clinical outcome measures included reduction of nasal polyps using the MacKay and Lund scoring system (Table 2) and improvement of symptom scores. Reduction of nasal polyps was defined as downgrade of polyp rating or decrease in size in those polyps that did not change in polyp grade.

Patients were seen at the clinic before, and a week after treatment and examined by the same physician. Nasal endoscopy was performed with a 30-degree Xenon sinuscope. Polyps were rated on the four-point grading scale proposed by MacKay and Lund[15] (Table 2). Pre- and post-treatment video recordings were rated by 3 independent observers.

Figure 1: Polyp grading

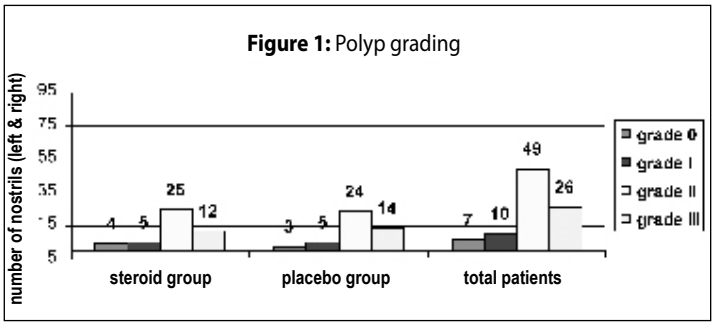

Figure 2-A: Reduction in polyp size in steroid group

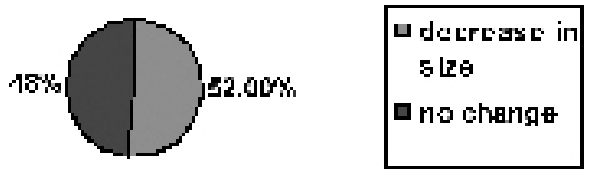

Figure 2-B: Reduction in polyp size in placedo group

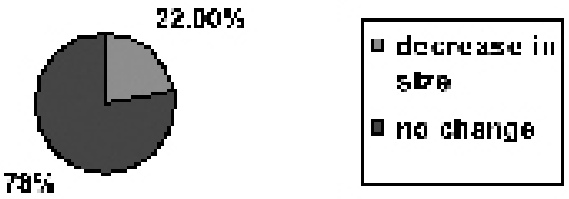

Table 5. Percentage of the different grades of polyps in total and in each group

	Total patients (both nostrils)	Medrol group (both nostrils)	Placebo group (both nostrils)
Grade 0	7.61%	8.70%	6.52%
Grade I	10.87%	10.87%	10.87%
Grade II	53.26%	54.35%	52.17%
Grade III	28.26%	26.09%	30.43%
Total	100%	100%	100%

Table 6. Size reduction of polyps

	Number of patients in steroid group	Number of patients in placebo group
Downgrade of polyp in both nostrils by 1 grade	8 (34.7%)	0
Downgrade of polyp in 1 nostril + decrease in size but still in initial grade in the other nostril	2 (8.70%)	0
Decrease in size but still in initial grade in both nostrils	2 (8.70%)	5 (21.74%)
No change	11 (47.83%)	18 (78.26%)
Total no. of patients with polyp reduction (in all degrees)	12 (52.17%)	5 (21.74%)
Total	23 (100%)t	23 (100%)

Table 7. Average change in polyp size

Steroid group	Placebo group
-15.8696	-2.6087

Fourteen symptoms associated with nasal polyps were assessed through a symptom scoring system ranging from 0 to 10, where a score of 0 corresponded to absence of symptoms and a score of 10 meant experiencing the worst symptoms (Table 3). All data was analyzed using SPSS for Windows version 9 statistics software package.

To be able to provide an analysis for the data on the decrease in polyp size, the following values were introduced as listed in (Table 4). A patient initially diagnosed to have a Grade II polyp would be given a score of 20. If after treatment the patient's polyp size improved from Grade II to Grade I, the patient would now have a score of 10 on the second visit. If the polyp grade did not change, but had a 30% size reduction, the score would decrease from 20 to 17.

RESULTS

There were a total of 48 patients in the study, 32 males (66.67%) and 16 females (33.33%). Two (2) were lost to follow up after the initial visit. Of the 46 remaining patients, 23 received methylprednisolone while the other 23 received placebo. On pretreatment endoscopic assessment, 7/46 (15.22%) had unilateral nasal polyps and 39/46 (84.78%) had bilateral polyps. Polyps were graded per nostril since half of the patients (50%) had different-sized polyps in each nasal cavity (Table 5). Grade 3 polyps were seen in 26/92 (28.26%) of the total number of nostrils examined during the initial consult. 49/92 (53.26%) had grade 2 polyps and 10/92 (10.87%) had grade 1 polyps. 7/92 (7.61%) of the nostrils had grade 0 polyps (Figure 1).

In the steroid group, 8 out of the 23 patients had a one step grade reduction in both nostrils (Table 6). Another 2 patients had a one step grade reduction in 1 nostril while the polyp in the other nostril remained in the same grade but had a 20% decrease in size. Two (2) patients had a 30-50% decrease of nasal polyp size in both nostrils while remaining in the original grade. In all, 12 patients (52.17%) had a reduction of nasal polyp size in various degrees after treatment with methylprednisolone. Using the Wilcoxon signed rank test, the reduction in nasal polyp size was statistically significant (0.002 and 0.004 in the right and left nostril respectively, at $P < .05$). There was an average 16% reduction in polyp size for patients who took methylprednisolone compared to the 3 %

reduction in those on placebo (Table 7).

In the placebo group, 5 patients out of the 23 (21.74%) had a 10-50% reduction in nasal polyp size after treatment but still remained in the initial grade. This decrease was not statistically significant (0.063 and 0.066 in the right and left nostril respectively, at 5% level of significance). Using the Mann-Whitney test, comparison of the size reduction between the 2 groups was statistically significant (0.015 and 0.034 in the right and left nostril respectively, at 5% level of significance).

Using the Wilcoxon signed rank test, the steroid group exhibited significant improvement in symptoms # 1 to 7, 9 to 11, 13 and 14 (headache, epistaxis, rhinorrhea, congestion, sneezing, itchiness, epiphora, post-nasal drip, throat discomfort, facial pain, fever and anosmia, at 5% level of significance). There was a slight improvement in symptom # 8 (cough, at 10% level of significance) and # 12 (eye complaints at 15% level of significance). In the placebo group, there was a significant improvement in symptoms #1 to 5, 7 and 10 to 12 (headache, epistaxis, rhinorrhea, congestion, sneezing, epiphora, throat discomfort, facial pain and eye complaints, at 5% level of significance). There was a slight improvement in symptoms # 6,9,13 and 14 (itchiness, post-nasal drip, fever and anosmia, at 10% level of significance). Using the Mann-Whitney test, the steroid group was shown to have a significant improvement in symptoms # 3, 4 and 14 (rhinorrhea, congestion and anosmia, at 6% level of significance) compared to the placebo group. There was also a slight improvement in treating symptoms # 8 and 9 with methylprednisolone than with placebo (cough and post-nasal drip, at 17% level of significance). There was no significant difference in improvement in the other symptoms between the 2 groups, nor were there adverse effects reported in either group.

DISCUSSION

The characteristics of the study population reflect those of patients with nasal polyps in the general population[16] with reference to age (mean age, 35.30 years) and male-to-female ratio (2:1).

The results of the study showed that there was a significant decrease in polyp size among patients in the steroid group by 1 grade. The volume of the polyps was reduced in 12/23 patients (52.17 %) by an average of 16%. Among these 12 patients, 10 reported general improvement in a majority of their symptoms based on the subjective clinical scoring system. There was also a significant difference when comparing the reduction in nasal polyps to that in the placebo group. These findings correspond to those of Damm et al.[9] where oral steroid therapy (oral fluocortolone 560 mg tapered for 12 days in group 1 and 715 mg tapered for 20 days in group 2) significantly reduced the extent of polyps on magnetic resonance imaging (>30%) in 50% of patients and diminished most sinus-related symptoms in 80% of the patients.

The symptom scores of the patients in both steroid and placebo groups improved for most symptoms. However, the steroid group had significantly better improvement in the symptoms of rhinorrhea, congestion and anosmia compared to placebo.

This study showed that a low dose, short-term treatment course of oral methylprednisolone (16mg a day for 7 days) can lead to significant reduction in the size of nasal polyps, and improvement of nasal symptoms of rhinorrhea, congestion and anosmia. This treatment course can also be used as a screening tool prior to prescribing intranasal steroid sprays, which are quite expensive. Non-responders can be referred for surgery, avoiding further costly medical management.

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