

Role of Macrolides on Management of Sinonasal Polyposis

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**Original
Article**

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ABSTRACT

Objective: This study aims to use macrolides as alternative to steroid in management of nasal polyposis.

Background: Allergic nasal polyps are benign and are characterized by mucosal inflammation and expansion into the lumen of the nasal cavity. The treatment of these lesions can include steroids, saline nasal spray, mucolytics, topical/systemic decongestants, topical anticholinergics, anti-leukotrienes or receptor blockers, and antihistamines, but steroids are the most effective drugs for medical polypectomy.

Patients and Methods: 96 patients with persistent bilateral nasal obstruction were included in our study during period from January 2017 to December 2018. 42 patients used oral steroid as group B and 54 patients used oral macrolides as group A. Patients were scheduled for follow-up visit (after three months) with respect to computed tomographic scan of paranasal sinuses scoring and endoscopic nasal scoring. The severity of polyposis was significantly lower in the macrolides group vs. the steroid group based on both radiological and endoscopic scoring. Non-significant difference detected in the patient satisfaction between both groups.

Conclusion: Macrolides are significantly effective drug in the management of nasal polyposis rather than steroid especially in cases contraindicated to use steroid in the regimen of management.

Key Words: Macrolides, nasal endoscopic, polyposis, steroid.

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INTRODUCTION

Nasal polyps (NP) are one of common benign nasal lesions could be occurred by mucosal inflammation affecting nasal mucosa. These nasal lesions appeared as pale grey protrusions extending outside the paranasal sinuses. In recent years, NP has been considered to represent a subgroup of chronic sinusitis. The most important factors in the development of nasal polyps are viewed as chronic inflammation and mucosal oedema, as well as bacterial or fungal infection may lead to basal polyposis^[1].

Nasal polyposis may be presented by nasal obstruction, smell disorders, facial headache or snoring, but the most common symptom is the nasal fullness. These lesions could be detected by anterior rhinoscopy, nasal endoscopy or as radiological findings^[2].

The purpose of NP treatment is to eliminate the polyps and to relieve the patient from the annoying symptoms. The medical treatment of NP needs longer duration and follow-up period. Medical or surgical treatment lines are two main options for management of NP, but the risk of recurrence is also existing with any line of management. The

medical treatment of NP can include the use of steroids, antibiotics, saline nasal spray, mucolytics, topical/systemic decongestants, topical anticholinergics, anti-leukotrienes, and antihistamines, but steroids are the most effective drugs known for NP treatment^[3].

Although beneficial, long-term oral steroid administration carries risk of potential side effects. Topical and oral steroid were used usually for management of nasal polyposis or the recurrent attacks of such disease. Steroid therapy reduces the inflammation and edema of nasal mucosa^[4].

Certain antibiotics such as macrolide antibiotics have been an anti-inflammatory effect so that it is thought to be effective in the management of NP but it is needed to be used for a long duration^[5].

The risk factors of prolonged intake of medical therapy that may lead to systemic diseases affect the decision of type of drugs to be taken. Steroid therapy may have long term complications as clouding of the lens in one or both eyes (cataracts), high blood sugar, which can trigger or worsen diabetes and increase risk of infections especially

with common bacterial, viral and fungal microorganisms. This study aims to find another alternative for steroid as prolonged therapy for NP^[6].

PATIENTS AND METHODS:

This prospective study was conducted in the period from January 2017 to December 2018 in the Department of Otolaryngology, Al Azhar University Hospitals. This study was approved by the ethical committee of the university. All patients were informed, and a written consent was obtained from all patients. The study included 96 patients aged between 18 and 50 years. They suffered from nasal obstruction as the main symptom as proven by history and examination. The diagnosis of NP was confirmed by nasoendoscopy or computed tomography (CT) of nose or paranasal sinuses. Patients were randomly subdivided into two groups according to line of medical therapy either steroid for group A (42 cases) or macrolides in group B (54 cases). Visual analogue score (VAS) was done to assess the nasal symptoms before any medical treatment. VAS test includes the degree of nasal obstruction, smell affection, the presence of productive cough and facial headache (each one of these symptoms give score from 0 to 5).

Both nasal cavities were assessed separately and scored according to the chronic rhinosinusitis staging system described in the guidelines for the European position paper on rhinosinusitis and nasal polyps 2012 (EPOS 2012)^[7]. The polyp sizes were evaluated from 0 to 3, with 0 being no polyp and 3 being polyps completely obstructing the nasal passage. The findings of oedema and discharge, as well as polyp sizes were scored between 0 and 2 according to their severity. Values in both nasal passages were collected, and the total score of both nasal cavities between 0 and 14 of all patients was recorded^[8].

The CT findings of the patients were evaluated according to the Lund-Mackay scoring system. This scoring system evaluates the occlusion of the osteomeatal complex and five major sinuses. The values on both sides were collected and the total scores were determined between 0 and 24^[8,9].

Topical steroid nasal sprays were used to all patients for twice daily for three months. Prednisolone treatment for group A was initiated by 1 mg/kg/day oral administration (divided into three doses over the day) as steroid therapy and then the dose was lowered to 10 mg every 1 week till the end to three weeks with the least dose 20 mg once daily. This group of patients received oral lansoprazole tablets to avoid gastric upset and an appropriate diet was recommended. 500 mg clarithromycin tablets were used as macrolide therapy for group B, it was given once per day for three weeks.

After one and three months, patient satisfaction and VAS was recorded to detect the quality of life after the

three months of medical treatment to NP. Also, scoring of nasoendoscopy for both nasal cavities and Lund-Mackay scoring system by CT nose was done after 3 months to evaluate the extent of NP.

Statistical Methods :

Descriptive statistics included the mean value and standard deviation. The t-test was used for quantitative analysis. The Chi-square test was used for the analysis of qualitative data. The SPSS 22.0 program was used for statistical analysis. So, the *p-value* was considered significant as the following: Probability (*P-value*): *P-value* 0.05 was considered insignificant.

RESULTS:

The age of the patients in group A ranged from 18 to 50 years old (with mean age 38.4 years); while the age in the group B ranged from 21 to 50 years old (with mean age 33.4 years). In the steroid group, 24 (57.1%) of 42 patients were men, while 29 (53.7%) of 35 in the macrolide group were men as shown in table 1 that shows patients baseline characteristics.

Table 1: Patient characteristic

Groups	Group A (N=42)	Group B (N=54)
Age	18-49 years old	21-50 years old
	Mean ±SD = 33.4 ±9.3	Mean ±SD = 38.4 ±10.8
Sex		
Male	24 (57.1%)	29 (53.7%)
Female	18 (42.9%)	25 (46.3%)

According to the endoscopic staging scores before treatment, there was no significant difference noted among both groups (*p*>0.05). On the otherwise, there were high significant differences showed between endoscopic staging scores before and after treatment to each groups (*p*<0.05). After treatment, endoscopic staging scores in the oral steroid group had significant difference compared to the scores of the macrolide group (Table 2).

Table 2: Endoscopic staging scores before and after treatment using t-test

Groups	Group A (N=42) Mean ±SD	Group B (N=54) Mean ±SD	<i>P-value</i>
Before treatment	10.3 ±2.3	9.9 ±2.1	0.332
After treatment	4.2 ±1.5	3.6 ±1.1	0.018
<i>P-value</i>	<0.001	<0.001	

There is no significant difference showed among both groups according to the radiological grading values before the treatment (*p*>0.05). Radiologic findings after

treatment in both groups showed high significant decrease in their scores compared to the scores before treatment for each group separately ($p < 0.001$). The radiologic grading score after treatment was significantly lower in the macrolide group than in the oral steroid group ($p < 0.001$) (Table 3, Figure 1 & 2).

Table 3: Radiologic grading scores before and after treatment using t-test

Groups	Group A (N=42) Mean \pm SD	Group B (N=54) Mean \pm SD	<i>P</i> -value
Before treatment	19.5 \pm 3.8	18.4 \pm 3.7	0.164
After treatment	14.8 \pm 4	13.3 \pm 3.3	0.042
<i>P</i> -value	<0.001	<0.001	

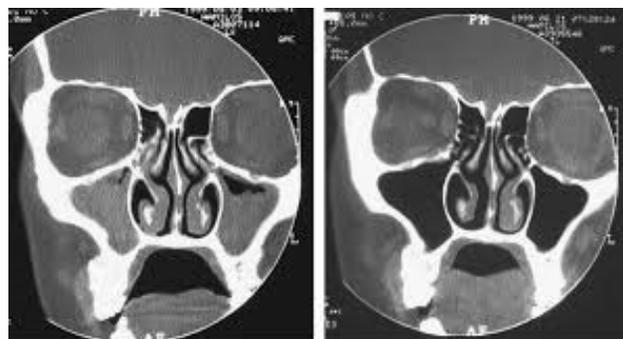


Fig.1: Pre- and posttreatment Paranasal sinuses CT in Group A. The left one is for pretreatment and the right one is for posttreatment



Fig. 2: Pre- and posttreatment Paranasal sinuses CT in Group B. The left one is for pretreatment and the right one is for posttreatment

Patient satisfaction showed non-significant difference between both groups after the three months of medical therapy either with oral macrolides or oral steroid ($p > 0.05$) as shown in (Table 4). There were many complications appeared in the fairly satisfied and unsatisfied patients as gastric upset and sore throat appeared after end of the treatment period. Figure 3 also shows mean VAS score diminish from 19.3 in group A up to 5.5 after steroid therapy. Mean VAS score diminish from 18.5 in group B up to 3.8 after macrolide therapy. There was non-significant difference between both groups ($p > 0.05$).

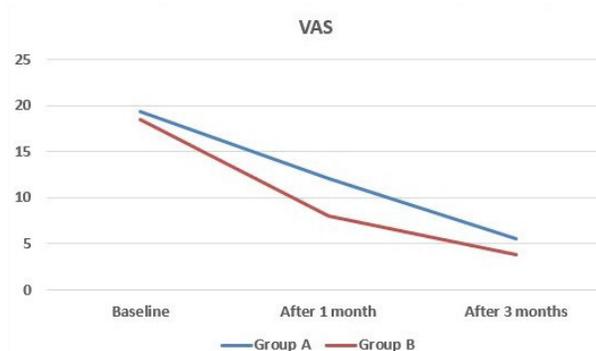


Fig. 3: VAS score at baseline and after one and 3 months

Table 4: Patient satisfaction after treatment using Q-square test

Groups/Patient satisfaction	Group A (N=42) Mean \pm SD	Group B (N=54) Mean \pm SD	<i>P</i> -value
Satisfied	34	41	0.961
Fairly satisfied	5	9	
Unsatisfied	3	4	

DISCUSSION

Steroid has the upper hand in management of patients with NP, but steroid therapy has many contraindication like Gastric ulcers, diabetic and hypertensive patients. Other medications could be offered to these patients with NP, such as topical anticholinergics, anti-leukotrienes or receptor blockers, antihistamines or saline nasal sprays, mucolytics, topical/systemic decongestants^[10].

Antibiotic treatment has not been considered an important alternative to steroid treatment in patients with NP, who have been treated as a subgroup of chronic rhinosinusitis in recent years^[11]. There is increasing evidence discussed the role of macrolides in treating nasal polyposis that they have both immunomodulatory effect and anti-inflammatory role in diminishing the chronic rhinosinusitis and lead to the concept of macrolides being immune-modulatory rather than anti-bacterial^[12].

Schalek *et al.*^[13] conducted a placebo-controlled study in which 23 patients who were serologically positive for enterotoxin-producing *Staphylococcus aureus* strains and scheduled for endoscopic sinus surgery were randomized to receive a 3-week oral anti-staphylococcal antibiotic treatment (quinolone, amoxicillin/clavulanate or co-trimoxazole) or a placebo. Both groups were evaluated preoperatively at three and six months with endoscopic polyp scores. The group using antibiotics showed better responses, but the differences did not reach the level of statistical significance.

By reviewing of the literature indicated that macrolide antibiotics have an anti-inflammatory effect on chronic inflammation in patients with NP when these antibiotics are used for a prolonged period. Yamada *et al.*^[14] treated 20 patients suffering from chronic rhinosinusitis and nasal polyps with clarithromycin (400 mg daily) for three months. In the group in which polyp sizes decreased, the interleukin-8 level decreased and their values had been significantly higher before macrolide treatment when compared to the group in which polyp sizes did not show any change.

Luo *et al.*^[15] administered a single dose of 250 mg clarithromycin daily for 12 weeks in 50 patients with chronic sinusitis (33 patients with chronic sinusitis without polyps and 17 patients with polyps). Comparison of the patients' visual analogue scores, endoscopic and radiological grading scores before and after treatment revealed significant improvement in all findings in both groups, but the improvement in the patients who had chronic sinusitis with polyps was more prominent.

In this study, patients treated with macrolides showed significant improvement in endoscopic and radiological staging after treatment. However, no definitive conclusion can be drawn regarding an antibiotic effect since all patients were administered nasal steroids and there was no control group. Van Zele *et al.*^[16] conducted a placebo-controlled trial to compare a 20-day administration of doxycycline (200 mg first, followed by 100 mg) and a 3-week treatment with methylprednisolone (1 week 32 mg, 1 week 16 mg and 1 week 8 mg) with the placebo. Inflammatory markers in the blood and nasal secretions were examined, polyp size was measured, and the symptoms were recorded. Methylprednisolone had a short but dramatic effect on polyp size and symptoms. During the 12-week study period, doxycycline also had a small but significant effect on the polyp size compared to the placebo. Doxycycline had a significant effect on postnasal efflux, but it did not change the other symptoms. Examination of the nasal secretions revealed that doxycycline reduced myeloperoxidase and eosinophilic cationic protein, as well as metaplastic protein 9. However, no quality-of-life measures was made, so it is not possible to determine whether doxycycline had an effect on the quality of life in this study group.

There is discrepancy between radiological and either patient satisfaction or VAS score. This could be explained due to the radiology analyses only the size and extent of nasal polyposis in the nasal and paranasal sinuses, but patient satisfaction or VAS were about the general condition or the nasal manifestation score of each patient not just the improvement of the nasal obstruction.

Kuran *et al.*^[17] added a treatment of clarithromycin 500 mg twice daily for three weeks to a group of patients with nasal polyps who had received systemic steroids, nasal steroids, and antihistamine treatment and did not significantly improve after steroid treatment. Symptomatic improvement was observed in 80% of the patients and radiological improvement in 40% of the patients with antibiotic treatment.

CONCLUSION

Significant differences were found between the steroid group and the macrolide group concerning radiological grading and endoscopic scoring. However, the difference between the two groups in terms of patient satisfaction was not statistically significant. So that, the use of antibiotics as macrolides could be used as another medical option to relief nasal obstruction in patients with NP especially in dealing with patients abounded for steroid prescription.

CONFLICT OF INTEREST

There are no conflicts of interest.

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