

## **Intrapolyp Corticosteroid Injection versus Oral Corticosteroid versus Topical Nasal Corticosteroid Spray in Treatment of Allergic Nasal Polyposis: Comparative Study**

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### **ABSTRACT**

**Background:** Nasal Polyposis are treated with topical steroids, systemic oral steroids, surgical excision, and intrapolyp steroid injection. Local and systemic steroid treatment is the mainstay of therapy for nasal polyposis.

**Objectives:** The aim of this study was to evaluate the role of intrapolyp steroid injection in the treatment of nasal polyposis and its efficiency, and to compare these results with that of oral and topical nasal spray corticosteroid.

**Patients and Methods:** This study involved 60 patients presented at ENT Outpatient Clinic, Al-Zahraa University Hospital and diagnosed as nasal polyposis. Their age ranged between (18-60) years. They were randomly divided according to type of treatment (nasal corticosteroid spray, oral corticosteroid and intranasal injection of corticosteroid) into 3 groups, each consisted of 20 patients.

**Results:** There were statistically significant differences in total nasal symptom score (TNSS), nasal polyp score (TNPS) and endoscopic analysis. It has been noted that in nasal spray group, Improvement of symptoms with No Regression of Polypis observed in 13 patients (65%) and no change at all in 7 patients (35%). While in oral steroids group, complete regression is observed in 4 patients (20%), partial improvement in 11 patients (55 %), and no response in 5 patients (25%) and in injection group, complete regression of polyps is observed in 2 patients (10%), partial improvement in 13 patients (65%), and no change at all in 5 patients (25%).

**Conclusion:** It could be concluded that intrapolyp steroid injection could be considered one of the alternative treatments of sinonasal polyposis as it is effective, easy, and safe procedure and its effect lasts for at least 3 months.

**Keywords:** Intrapolyp Corticosteroid Injection, Oral Corticosteroid, Topical Nasal Corticosteroid Spray, Allergic Nasal Polyposis.

### **INTRODUCTION**

Patients with nasal polyposis often experience severe nasal obstruction, anosmia, nasal crusting, Facial pain or headache, Snoring, Loss of sense of taste and chronic rhinosinusitis (CRS), and have been shown to carry a significantly greater health burden than patients with chronic rhinosinusitis, without polyposis. Studies have demonstrated that patients suffering from CRS with nasal polyposis score worse on quality of life questionnaires than patients with coronary artery disease, chronic obstructive pulmonary disease and congestive heart failure<sup>(1)</sup>.

Treatment options vary and range from, local and systemic medications to surgical removal often including endoscopic sinus surgery<sup>(2)</sup>.

Although surgical treatment may be needed when the bulk of polyps is excessive, medical therapy can be used to manage cases successfully. In addition, surgery carries a lot of potential complications including CSF leak, pnuemocephalus, permanent diplopia and blindness, with estimated overall rate at roughly 1% for experienced surgeons, as well as the risk of

intra- and perioperative major medical complications which are secondary to the general stress of surgery and anesthesia as myocardial ischemia and infarcts, metabolic acidosis, cardiac arrhythmias, stroke, seizures, and severe hypotension<sup>(3)</sup>.

The mainstay of contemporary medical treatment of polyps continues to be intranasal and oral systemic corticosteroids<sup>(4)</sup>.

Intranasal steroid sprays, even though used very frequently, sometimes fail to provide symptomatic improvement and their use can be complicated by a perforation of nasal septum<sup>(5)</sup>.

**Alobid et al.**<sup>(6)</sup> showed the benefit of short-term oral steroids in patients with nasal polyposis. Any consideration of systemic steroids, however, must include screening of patients for relative contraindications as well as informing them of potential systemic side effects.

There is another method of treatment for nasal polyposis which is intranasal corticosteroid injection. However, in 1962, the first instance of permanent visual loss was reported after intranasal injection of steroid, followed by some other reports

in the following years. This made the physicians to become wary about this technique. Since these publications, several authors have published their results representing more than one hundred thousand intranasal corticosteroid injections (polyp or nonpolyp), with no instances of reported visual loss. So, there is a high degree of controversy on the safety of intranasal steroid injection, mostly based on visual loss <sup>(2)</sup>.

Although many studies were conducted to verify the efficacy and safety of intrapoly steroid injection, there is limited studies that compare the efficacy and side effects of intrapoly steroid injection versus oral steroid administration <sup>(7)</sup>.

The aim of this study was to evaluate the role of intrapoly steroid injection in the treatment of nasal polyposis and its efficiency, and to compare these results with that of oral and topical nasal spray corticosteroid.

## PATIENTS AND METHODS

This comparative prospective study included a total of 60 patients diagnosed as allergic nasal polyp, attending at ENT Outpatient Clinic, Al-Zahraa University Hospital. This study was conducted between March 2018 to November 2019.

### Ethical Considerations:

**Approval of the Ethical Committee of Faculty of Medicine, Al-Azhar University was obtained.** Written informed consent had been obtained from all participants. Every patient was free to refuse participation in the study without affecting the service or the clinical management. They are free to ask any question about the study.

### Inclusion criteria:

- Age range from (18-60) years old.
- Patients should have allergic nasal polyp.

### Exclusion criteria:

- Patients with other causes of nasal polyp eg. cystic fibrosis, ciliary dyskinesia.
- Any condition contraindicating intake of steroids eg. (diabetes, hypertension, congestive heart failure, osteoporosis, glaucoma, pregnancy, peptic ulcer, tuberculosis, and herpes simplex keratitis)
- Patients with history of previous sinus surgery
- Patients who took corticosteroids orally or parenterally
- Patients with eye problems eg. hypertelorism or proptosis.

Patients age ranged between (18-60) years and they were 33 males and 27 females. The included

subjects were randomly divided according to type of treatment (nasal corticosteroid spray, oral corticosteroid and intranasal injection of corticosteroid) into three groups; **Group 1 (intrapoly corticosteroid injection)** consisted of 20 patients. They received intrapoly corticosteroid injection (1ml diprofos injection each ml contain betamethasone sodium phosphate 2.63 mg (eq.to betamethasone 2 mg) +betamethasone dipopionate 6.43mg (eq. to betamethasone 5 mg)) for up to three times with intervals of 1 month., **Group 2 (oral corticosteroid)** consisted of 20 patients. They received oral corticosteroid (the patients received oral prednisolone for four weeks starting with dose of 1mg/kg/day and decreasing the dose by 20 mg every 5 days and the last 5 days received 5mg/kg/day) and **Group 3 (nasal spray)** consisted of 20 patients. They received fluticasone propionate aqueous nasal spray (FPANS) 100 microg twice daily twice daily for 12 weeks.

- In injection group,
  - 1ml diprofos injection was used for injection using a 100 unit insulin syringe and 21 gauge needle or larger.
  - 4% lidocaine was sprayed into the nasal cavity before the injection.
  - Cotton pledgets soaked in lidocaine were then packed into the nasal cavity.
  - The cotton was removed, and the needle was slightly bent at the hub to allow for better visualization.
  - The diprofos was injected into the polyp with depth of 1 – 2 mm using 0-degree endoscope.
  - The 1ml of diprofos was shared among the polyps, and not more than 0.5 ml was injected in a single polyp due to the runoff.
  - The majority of the patients received injections bilaterally. The patients returned at a month interval till they completed a series of three injections.
- All patients in the study were assessed before starting the treatment using total nasal symptom score (TNSS), endoscopic examination using total nasal polyp score (TNPS) and CT imaging using Radio endoscopic analysis were used for the assessment.

### Radio endoscopic analysis:

The CT imaging of paranasal sinuses were evaluated using Radio endoscopic analysis system and scored on a 0 to 4 scale as follows:

**Grade 0:** partial thickness of the sinus or complete improvement.

**Grade 1:** nasal polyp is intrasinus.

**Grade 2:** extended to lower limit of inferior border of middle turbinate.

**Grade 3:** extended to superior border of inferior turbinate.

**Grade 4:** extended to inferior border of inferior turbinate and floor of the nose.

**Follow up:**

All patients were assessed 3 months after all modalities of treatment using TNSS, TNPS and radio endoscopes analysis. Results after 3 months were compared with parameters before starting treatment and results of injection were compared with that of oral steroids and topical nasal steroid spray

**Statistical analysis**

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

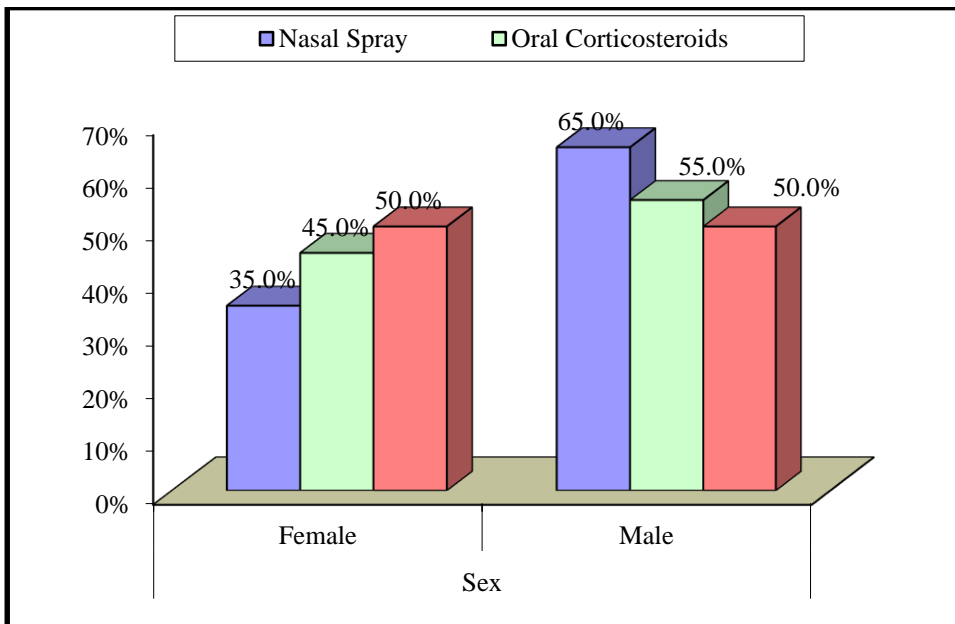
**The following tests were done:**

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square ( $\chi^2$ ) test of significance was used in order to compare proportions between two qualitative parameters.

- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following:
- Probability (P-value)
  - P-value <0.05 was considered significant.
  - P-value <0.001 was considered as highly significant.
  - P-value >0.05 was considered insignificant.

**RESULTS**

- The demographic characteristics of the 60 patients, there were 13 males and 7 females in the nasal steroid spray, 11 male and 9 female in the oral steroids group and 10 males and 10 females in the injection group, with age range from 18 -55 years in all groups. 4 patients in the nasal corticosteroid spray and 1 patient in the oral steroids group were asthmatic, No one in injection group was asthmatic. A total of 60 injections were administered in 20 patients, 20 patients received 60 mg oral prednisolone with gradual tapering over 4 weeks, and 20 patients received fluticasone propionate aqueous nasal spray (FPANS) 100 microg twice daily for 12 weeks.



**Figure (1):** Graph showing Males and Females percentage among the three groups

**Table 1:** TNSS in the three groups Before and after receiving treatment.

TNSS		Nasal Spray		Oral Corticosteroid		Corticosteroid Injection		Test value*	P-value	Sig.
		No.	%	No.	%	No.	%			
Before TTT	0	0	0.0%	0	0.0%	0	0.0%	10.303	0.112	NS
	1 to 2	6	30.0%	0	0.0%	5	25.0%			
	2 to 3	2	10.0%	0	0.0%	2	10.0%			
	3 to 4	10	50.0%	16	80.0%	10	50.0%			
	5 to 6	2	10.0%	4	20.0%	3	15.0%			
After TTT	0	0	0.0%	2	10.0%	8	40.0%	13.992	0.030	S
	1 to 2	13	65.0%	11	55.0%	7	35.0%			
	2 to 3	0	0.0%	0	0.0%	0	0.0%			
	3 to 4	5	25.0%	5	25.0%	2	10.0%			
	5 to 6	2	10.0%	2	10.0%	3	15.0%			
<b>Chi-square test</b>		<b>6.246</b>		<b>19.429</b>		<b>15.667</b>				
<b>P-value</b>		<b>0.182</b>		<b>0.001</b>		<b>0.004</b>				

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)  
 \*:Chi-square test

TNSS of the three groups were not significantly different before treatment .  
 After treatment, the nasal spray group were not statically significant while oral corticosteroid groups and injection groups showed highly statistically significant , with no significant difference in the three groups scores at the end of the treatment (table 1 )

**Table 2:** TNPS in the three groups Before and after receiving treatment.

TNPS		Nasal Spray	Oral Corticosteroids	Corticosteroid Injection	Test value‡	P-value	Sig.
		No. = 20	No. = 20	No. = 20			
Before TTT	Median(IQR)	2 (1 - 2)	2 (2 - 3)	2 (2 - 3)	4.336	0.114	NS
	Range	1 - 3	1 - 3	1 - 3			
After TTT	Median(IQR)	2 (2 - 3)	2 (1 - 2)	1 (1 - 2)	7.108	0.029	S
	Range	1 - 3	0 - 3	0 - 3			
<b>Wilcoxon Rank test</b>		<b>-1.394</b>	<b>-3.314</b>	<b>-3.500</b>			
<b>P-value</b>		<b>0.163</b>	<b>0.001</b>	<b>0.000</b>			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)  
 ‡: Kruskal Wallis test

TNPS of the three groups were not significantly different before treatment .  
 After treatment, the nasal spray group were not statically significant while oral corticosteroid groups and injection groups showed highly statistically significant , with no significant difference in the three groups scores at the end of the treatment (table 2 ).

**Table 3:** Radio Endoscopic analysis before and after treatment in the three groups.

Radio Endoscopic Analysis		Nasal Spray	Oral Corticosteroids	Corticosteroid Injection	Test value‡	P-value	Sig.
		No. = 20	No. = 20	No. = 20			
Before TTT	Median(IQR)	3 (3 - 3)	3 (2 - 3)	3 (2 - 4)	3.198	0.202	NS
	Range	3 - 4	2 - 4	2 - 4			
After TTT	Median(IQR)	3 (3 - 3)	2 (1 - 3)	2 (1 - 3)	16.385	0.000	HS
	Range	3 - 4	0 - 4	0 - 4			
<b>Wilcoxon Rank test</b>		<b>0.000</b>	<b>-2.558</b>	<b>-3.573</b>			
<b>P-value</b>		<b>1.000</b>	<b>0.011</b>	<b>0.000</b>			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)  
 ‡: Kruskal Wallis test

Radio Endoscopic Analysis of the three groups were not significantly different before treatment (table3). After treatment, the three groups showed Highly statistically significant, ( $p < 0.000$ ) as shown in table, At the end of the treatment nasal spray group was not significantly different ( $p = 1.00$ ) , oral corticosteroid group showed a statistically significant, ( $p = 0.011$ ) and The injection group showed highly statistically significant ( $p = 0.000$ ) (table 3).

**Table 4:** Percentage of complications in injection group.

Complication	Percentage
Hypertension	0%
Hyperglycemia	0%
GIT upsets	0%
Mood changes	0%
Visual disturbance	0%
Bleeding	3%
Facial flushing	0%

No serious complications as hypertension, hyperglycemia, GIT upsets or mood changes, were reported in nasal spray group and oral steroids group. In injection group, no serious complications as visual disturbance, severe bleeding, or facial flushing were observed apart from mild self-limited bleeding detected in only 2 injections(3.3%) of all 60 injections (table 4).

## DISCUSSION

The aim of this study was to evaluate the role of intrapoly steroid injection in the treatment of nasal polyposis and its efficiency, and to compare these results with that of oral and topical nasal spray corticosteroid.

This study included 60 patients, their age ranged between (18-60) years. Patients were divided into 3 groups each group have 20 patients.

As regard gender, there were 33 male and 27 female distributed as follow: 13 males (65%) and 7 females(35%) in the nasal steroid spray group, 11 male(65%) and 9 female(45%) in the oral steroids group and 10 males(50 %) and 10 females(50%) in the injection group.

As regard age and gender, there were no statistically differences between three groups.

Regarding to nasal steroid spray group patient, they didn't show improvement in nasal symptoms and polyp size, with no statistically differences in TNSS, TNPS and Endoscopic analysis.

These findings matched with those of **Aouad and Chiu** <sup>(8)</sup> and **Small et al.** <sup>(9)</sup> who showed that topical steroids need long period to be

effective. In addition, some patients didn't respond to topical steroids, and authors explained this as nasal congestion by nasal polyps causes inadequate intranasal distribution of topical steroids <sup>(10)</sup>.

In contrast with **Joe et al.** <sup>(11)</sup>, demonstrated in a randomized, double-blind placebo-controlled study the efficacy of intranasal steroid sprays. In their study, 157 patients with bilateral nasal polyposis were randomized to receive nasal steroid spray or placebo. Patients who received steroids showed statistically and clinically significant improvement in nasal symptoms and polyp size when compared to those who received placebo

**Chong et al.** <sup>(12)</sup> also demonstrated the efficacy and tolerability of daily intranasal corticosteroids spray in patients with nasal polyps. However, the risk of adverse effects such as epistaxis and local irritation is increased in people taking intranasal corticosteroids. So, application of nasal steroid spray has been proposed to be an alternative delivery method to provide maximum effect in the middle meatal area <sup>(13)</sup>.

This matching with **Hissaria et al.** <sup>(14)</sup> who found that Systemic steroids have been shown to be highly effective in chronic sinusitis with polyps. A double-blind, placebo-controlled study reported a significant effect of 14 days of therapy with 50 mg prednisolone on nasal polyp size and symptoms (on the basis of a standardized patient questionnaire) compared with placebo.

This also matching with **Muzaffer et al.** <sup>(15)</sup> who found that systematic steroid effective method of treatment of nasal polyp, study reported significant decrease in symptom score , polyp score and ct score .

As regard intrapolyop injection group, 1ml diprofos (betamethasone) were used in 60 injections for 20 patients, all injections were intrapolyop with average number of 3 injections for each patient, there were 10 female patients (50%) and 10 male patients (50%) with age range (18-60) with mean age 34,2.

75% of the patients in injection group in our study showed clinical improvement(10% complete improvement and 65% partial improvement), and almost all of them needed 3 injections for improvement.

There were statistically different in TNSS, TNPS and endoscopic analysis.

**Moss et al.** <sup>(16)</sup> and **Kiris et al.** <sup>(7)</sup>, both used, triamcinolone acetone in the injection, both polyps and turbinates were targets for injection, In the present study, the study population included only patients with sinonasal polyposis, and this is similar to the target population in **Kiris et al.** <sup>(7)</sup> study, while in **Moss et al.** <sup>(16)</sup> study, the injection

was carried for patients with chronic sinusitis with or without polyps.

In **Moss et al.** <sup>(16)</sup> study, triamcinolone acetonide was used in 237 injections for 78 patients, of which 152 were intratubinal and 85 were intrapolyp in 25 patients, with average number of 3 injections for each patient, there were 48 male patients (62%) and 23 female patients (38%) with age range (19-91) with mean age of 60.4.

Matching with our study **Moss et al.** <sup>(16)</sup> study stated that the percentage of patients that reported improvement from injections is 84.5%, and the average number of injections received by them is 3 injections. In the mentioned study, assessment of the response to treatment was based on symptomatic base only, subjectively without using any scores.

In comparison between the three groups of treatment we used TNSS, TNPS and endoscopic analysis.

In nasal spray group (20 patients) there is no statistically significant differences in TNSS, TNPS and radio endoscopic analysis.

Comparing to oral steroid group (20 patients) that showed significant decrease in TNSS with improvement 75% of patients, TNPS with improvement 65% of patients and radio endoscopic analysis with improvement 40% of patients.

Comparing to injection group that showed significant decrease in TNSS with improvement 55% of patients, TNPS with improvement 65% of patients and radio endoscopic analysis with improvement 75% of patients and all patients received 3 injection for improvement with total 60 injection for 20 patients.

There are limited studies that compare the efficacy of the steroid injection versus oral steroids versus nasal spray, one study **Kiris et al.** <sup>(7)</sup>, was conducted on ninety patients showed that there is significant decrease in TNSS and TNPS of the patients that received injection steroids, with improvement of 82.2% in TNPS, and most patients received 5 injections for improvement with total 211 injections.

Comparing to systemic steroids, **Kiris et al.** <sup>(7)</sup> found that a slightly higher number of patients improved in oral steroid group representing 86.7% of the patients. But this difference was not statistically different in **Moss et al.** <sup>(16)</sup> study, showing that intrapolyp steroid injection is comparable to the high efficacy of oral steroids observed in these studies.

In the present study It has been noted that in nasal spray group, Improvement of Symptoms with No Regression of Polyp is observed in 13 patients (65%) and no change at all in 7 patients

(35%). while in oral steroids group, complete regression is observed in 4 patients (20%), partial improvement in 11 patients (55 %), and no response in 5 patients (25%) and in injection group, complete regression of polyps is observed in 2 patients (10%), partial improvement in 13 patients (65%), and no change at all in 5 patients (25%).

In addition to well-known steroid administration methods, intrapolyp steroid injection represents a potential method to deliver high concentrations of this anti-inflammatory drug to a local area <sup>(17)</sup>, thus it is supposed to have more effect than topical steroids. In other words, it is thought to combine the efficacy of oral steroids to the limited side effect of topical steroids. Moreover, the effect of single injection seems to last for 6-8 weeks, largely due to the depot nature of the suspension <sup>(18)</sup>, and this result is comparable to what was found in this present study during 3 months follow up. Also, the intrapolyp steroid injection is typically an office based procedure that takes approximately 2-3 minutes.

Recurrence wasn't reported during the 3 month interval of this study in both groups, while **Kiris et al.** <sup>(7)</sup> and **Ulku et al.** <sup>(19)</sup> didn't observe recurrence for at least 6 months and **Camp et al.** <sup>(20)</sup> showed that polyps tended to recur after 5 months of treatment with oral prednisolone. However, in **Thibaut et al.** <sup>(21)</sup>, total recurrence was noted after 3 months of short-term oral steroid therapy in all patients. This may be attributed to the small dose of corticosteroids used in the later study.

It has been noted in this discussed study that there is disparity between the symptoms and findings observed in endoscopy and CT after treatment. As it was observed that the improvement in the symptoms is much more obvious than endoscopic and CT findings. This observation was noted in **Ulku et al.** <sup>(19)</sup> study, and this reflect that despite the previously mentioned encouraging results representing a great clinical improvement, neither oral steroids nor intrapolyp injection can eradicate the polyps. This raises the concern of recurrence of symptoms and regrowth of polyps beyond the interval of the study, which may necessitate endoscopic surgery later on. But at the same time, it can be the only effective option in some patients that are not fit for surgery and oral steroids are contraindicated for them.

Loss of smell is a major disabling complaint in patients with nasal polyposis <sup>(6)</sup>. Surgery has no beneficial effect on hyposmia. This may be due to the fact that hyposmia is related to mucosal inflammation rather than volume changes caused by the polyps and olfactory impairment in IgE mediated nasal allergy is highly correlated to the degree of inflammation of the mucosa <sup>(22)</sup>.

We didn't observe any serious complications after treatment such as anxiety, palpitation, visual disturbance, major bleeding or visual complications. Only minor self-limited bleeding was noticed in only 2 injections out of 60 injection (3%). Minor bleeding was also seen in 6 out of 211 injections (0.03%) in **Kiris et al.** <sup>(7)</sup> study. An attack of acute anxiety and palpitation was reported in one injection out of 237 injections (0.4%) in **Moss et al.** <sup>(16)</sup> study.

In a recent study, intranasal steroid injection was found to be safe when performed properly **Moss et al.** <sup>(16)</sup> estimating the risk of the visual disturbance as 0.003%, compared to 0.00% in this study and **Kiris et al.** <sup>(7)</sup> study.

It has been thought that the most likely etiology of visual loss in these patients involved retinal embolization and vasospasm <sup>(18)</sup>. Retrograde embolization may occur when the steroid particles flow reversely through the anterior or posterior ethmoid arteries to the ophthalmic artery, and then into the central retinal artery where they cause a vaso-occlusive event <sup>(23)</sup>.

Finally, this current study has some limitations. The sample size was relatively small and time of follow up was short, so recurrence beyond 3 months couldn't be assessed. In addition, combination of injection with short course of oral steroids or combination of injection with local nasal sprays wouldn't tested in this study, which is assumed to be more effective and delay the time of recurrence. Another limitation is that laboratory analysis of steroid level wasn't done in this study to evaluate the systemic absorption of steroids after local injection although it was found to be within normal in other studies. Finally, more than three injections wasn't tried in this study which was found to be more effective in some refractory cases in other studies in which response was noted after four and five injections.

## CONCLUSION

It could be concluded that intrapolyp steroid injection could be considered one of the alternatives in the treatment of sinonasal polyposis, as it is an effective, easy, and safe procedure and its effect lasts for at least 3 months. It was proven to show comparable results to oral steroids as both modalities showed a statistically significant improvement subjectively and objectively as well in CT imaging's.

However, cases with extensive bulky polyposis were resistant to complete eradication by injection and they may need surgical intervention later on. This and previously conducted studies proved that no visual complications as well as other

minor complications could threaten this procedure as long as proper technique is ensured.

Further studies are needed to study the effect of larger number of injections and longer duration of action than this current study, in addition combination with intranasal sprays is needed to be tested.

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