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Does the Preoperative Administration of Steroids Reduce Intraoperative Bleeding during Endoscopic Surgery of Nasal Polyps?

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Abstract

Objectives. Corticosteroids are frequently used in a range of otorhinolaryngologic conditions due to their anti-inflammatory and antiedematous properties. In this meta-analysis, we aimed to assess the role of preoperative steroids for attenuating intraoperative bleeding during endoscopic sinus surgery among patients with nasal polyps.

Data Sources. PubMed, SCOPUS, EMBASE, the Web of Science, and Cochrane database.

Methods. Literature was screened from January 1980 to January 2016. Five articles comparing patients who were preoperatively administered steroids (steroid groups) with patients who received a placebo or no treatment (control group) were included for analysis, which encompassed intraoperative bleeding, endoscopic surgical field visibility, operative time, and side effects during endoscopic sinus surgery.

Results. Intraoperative bleeding and operative time during endoscopic sinus surgery in the steroid group were significantly reduced as compared with the control group. Additionally, the preoperative administration of steroids had a significant effect on improving endoscopic surgical field visibility during sinus surgery. There were no significant adverse effects reported in the enrolled studies. In subgroup analyses of these results, steroids showed similar effects on intraoperative bleeding regardless of administration type (topical or systemic).

Conclusion. This study demonstrated that the preoperative administration of steroids in patients with nasal polyps could effectively reduce intraoperative bleeding. However, the duration of treatment and dosing standard require further investigation, and more trials need to be included.

Keywords

steroid, nasal polyp, bleeding, surgical field, operative time, meta-analysis

Nasal polyps are common benign outgrowths of tissue into the nasal cavity. They are of unknown etiology, and they are usually found in association with chronic rhinosinusitis.[1] Although the management of chronic rhinosinusitis with nasal polyps remains controversial, endoscopic sinus surgery (ESS) is considered to be the procedure of choice for the surgical management of chronic rhinosinusitis with nasal polyps refractory to medical approaches, such as intranasal or systemic steroids.[2] However, given the vascularity of the paranasal sinuses, particularly during infectious states, even a small amount of hemorrhage can greatly affect visibility and, thus, the overall surgery. Sinus surgeons use a multitude of techniques in an attempt to diminish intraoperative hemorrhage. However, there has not been a consensus on the ideal strategy to decease intraoperative bleeding during sinus surgery.[3]

Corticosteroids are frequently used in a range of otorhinolaryngologic conditions due to their anti-inflammatory properties.[4] Corticosteroids are currently utilized to induce remission and control nasal polyps, with few side effects; they are also useful for their ability to prevent or delay the recurrence of nasal polyps after surgery.[1] Several recent studies have observed the positive effects of preoperative steroid administration on intraoperative bleeding during ESS. However, the current evidence in the literature is not sufficient to advocate for the preoperative administration of steroids to control intraoperative bleeding in ESS. Given that ESS is a popular operation and intraoperative bleeding is a frequent event during ESS in patients with nasal polyps,

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it is essential that surgeons follow effective practices for reducing intraoperative morbidity. The aim of this review was to evaluate the evidence for the effects of steroids on the outcomes of patients with nasal polyps who are undergoing sinus surgery.

Materials and Methods

Search Strategy and Study Selection

Clinical studies published in English were identified from PubMed, SCOPUS, EMBASE, the Web of Science, and the Cochrane Register of Controlled Trials up to the cutoff publishing date of January 2016. The following search terms were used: ''nasal polyp,'' ''endoscopic sinus surgery,'' ''steroids,'' ''bleeding,'' ''surgical field,'' and ''operation time.''

Two reviewers, working individually, screened all abstracts and titles for candidate studies and dropped those that were not associated with the preoperative administration of steroids. Full texts of potentially relevant studies were obtained if a decision for inclusion could not be made from the abstract alone. The next inclusion criterion was prospective controlled trials that studied patients undergoing ESS and preoperatively administered steroids, regardless of administration type. Studies were not deemed appropriate for inclusion if, in addition to sinus surgery, the patients underwent procedures such as septal and turbinate surgery or if the reports were duplicated. Additionally, studies were excluded from the analysis if the outcomes of interest were not clearly provided with quantifiable data or if it was impossible to evaluate the appropriate data from the published results. **Figure 1** summarizes the search strategy used to identify the studies selected for meta-analysis.

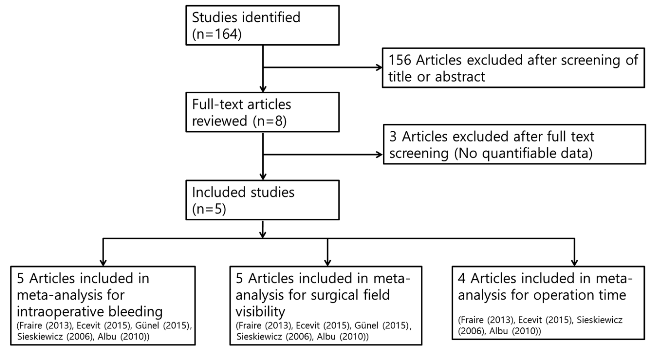

Figure 1. Study selection diagram.

Data Extraction and Risk of Bias Assessment

Data from eligible studies were extracted via standardized forms and checked by the 2 reviewers individually. Analyzed outcomes were operative blood loss,[5-9] operative field visibility,[5-9] operation time,[5,6,8,9] and adverse events related to steroid administration. These outcomes were compared in the preoperative steroid group (including oral or topical administration) versus the control group (patients receiving a placebo or no treatment) during the operation and postoperative period.

We selected data with respect to patient number, operative field visibility–related grading scale, quantity of operative bleeding and time, and occurrence rate of side effects, and the *P* value was reported as a comparison of the preoperative steroid group with the control group from the studies marked for inclusion. This was done to determine the influence of the administered steroid on operative bleeding and adverse effects.

Analyses for Statistics

The statistical analysis of the included studies was conducted through the R program (R Software Foundation, Vienna, Austria). In the case of quantitative variables, meta-analysis was conducted with the standardized mean difference (SMD). The SMD is adopted as a summary statistic to standardize the results of the studies to an equal scale when the studies measure an equal outcome but assess it with various methods. This method was selected to analyze operative blood loss, operative field visibility, and operative time because there was no single standardized scale used in all studies. We concurrently used a funnel plot and Egger's test to identify potential publication bias. In addition, we used Duval and Tweedie's trim and fill to compensate for the summed effect size with respect to publication bias.

Results

Five studies with 187 participants were included and reviewed for the meta-analysis. The results of the bias evaluations and study characteristics are shown in **Tables 1** and **2**. Publication bias was not analyzed, because the number of enrolled trials was not sufficient to analyze a funnel plot.

Effect of Preoperative Steroids versus Control

Operative bleeding (SMD = −0.60; 95% confidence interval [95% CI]: −1.09, −0.11), operative field visibility (SMD = −0.85; 95% CI: −1.32, –0.36), and operative time (SMD = −0.84; 95% CI: −1.26, −0.43) were statistically lower in the steroid group than in the control group. Significant interstudy heterogeneity ($I^2 > 50\%$) was found for operative bleeding ($I^2 = 61\%$) and operative field visibility ($I^2 = 58\%$), though not for operative time ($I^2 = 19\%$; **Figures 2-4**).

The side effects of steroids administration reported in a single study included nasal irritation, nasal dryness, and throat discomfort caused by topical administration. Therefore, there were not enough data to conduct the meta-analysis.

Subgroup Analysis according to Operation Type

The overall analysis included all types of steroids without taking into account the route, such as systemic or topical application. This could explain the high heterogeneity in operative bleeding and operative field visibility. Consequently, subgroup analyses were applied (**Table 3**). There was a significant difference in the probability of obtaining a result (*P* value or confidence interval) for

Table 1. Characteristics of Studies Included in the Meta-analysis.

Study	Sample Size, n	Comparison	Outcome Measures Analyzed	Judgment of Risk of Bias
Fraire (2013)[5]	31	Preoperative steroid vs control (systemic)	Intraoperative bleeding (the amount of blood in the suction bottle during surgery; mL) Surgical field visibility (6-point scale by Boezaart et al) Operative time (min)	High
Ecevit (2015)[6]	22	Preoperative steroid vs control (systemic)	Intraoperative bleeding (the amount of blood in the suction bottle during surgery; mL) Surgical field visibility (6-point scale by Boezaart et al) Operative time (min)	Low
Günel (2015)[7]	65	Preoperative steroid vs control (systemic)	Intraoperative bleeding (the amount of blood in the suction bottle during surgery; mL) Surgical field visibility (10-point linear scale)	Low
Sieskiewicz (2006)[8]	36	Preoperative steroid vs control (systemic)	Intraoperative bleeding (the amount of blood in the suction bottle during surgery; mL) Surgical field visibility (6-point scale by Boezaart et al) Operative time (min)	Low
Albu (2010)[9]	33	Preoperative steroid vs control (topical)	Intraoperative bleeding (the amount of blood in the suction bottle during surgery; mL) Surgical field visibility (6-point scale by Boezaart et al) Operative time (min)	Low

Table 2. Studies Included in the Meta-analysis.

Study	Patients (n) and Type of Surgery	Level of Evidence	Administration of Steroid Therapy	Finding
Fraire (2013)[5]	Steroid (14) vs control (17) Primary surgery	Level II (nonrandomized controlled prospective study)	30 mg/d of oral meprednisone, divided in 2 Doses for 5 consecutive days prior to ESS	Only operative bleeding significantly reduced in patients with chronic rhinosinusitis with nasal polyps
Ecevit (2015)[6]	Steroid (10) vs control (12) Primary surgery	Level I (randomized controlled prospective study)	10 mg of oral prednisolone for the first 7 d, then tapered down and stopped on day 17 prior to ESS	Intraoperative bleeding, surgical field visibility, and operative time significantly improved
Günel (2015)[7]	Steroid (32) vs control (33) Primary surgery	Level I (randomized controlled prospective study)	1 mg/kg of oral prednisolone for 2 d, then tapered down and stopped on day 10 prior to ESS	Oral corticosteroids not necessary in the preoperative period
Sieskiewicz (2006)[8]	Steroid (18) vs control (18) Primary surgery	Level I (randomized controlled prospective study)	30 mg of oral prednisone for 5 consecutive days prior to ESS	Surgical field visibility significantly improved
Albu (2010)[9]	Steroid (17) vs control (16) Primary surgery	Level I (randomized controlled prospective study)	200 μg of topical mometasone furoate spray twice daily for 4 wk prior to ESS	Intraoperative bleeding, surgical field visibility, and operative time significantly improved

Abbreviations: ESS, endoscopic sinus surgery.

operative bleeding between the 2 groups, which could explain the high heterogeneity of this measurement. For operative field visibility and operative time, the analysis of effect according to the type of the administration suggested that this factor did not have a significant effect on the analyzed outcomes.

Discussion

The outcome of ESS depends on many factors, with one of the most important being a clean surgical field during the procedure.[9] Because of the anatomic characteristics of the sinonasal area, bleeding (regardless of its rate) can be enough to limit the visual field and increase the risk of

Study	Steroid total	control total	Weight	Std. Mean Difference, Random, 95 % CI
Fraire (2013)	14	17	19.0 %	-0.82 [-1.55, -0.09]
Ecevit (2015)	10	12	16.5%	-1.02 [-1.87, -0.17]
Günel (2015)	33	32	25.1 %	0.17 [-0.31, 0.65]
Sieskiewicz (2006)	18	18	20.3%	-0.63 [-1.31, 0.05]
Albu (2010)	17	16	19.1 %	-1.01 [-1.74, -0.28]
Total (95 % CI)	**74**	**96**	**100 %**	**-0.60 [-1.09, -0.11]**

Heterogeneity : Q(df = 4) = 11.5898, *P* val = .0207, I^2 = 61.76 %

Test for overall effect : Z = -2.3988 (*P* = .0164)

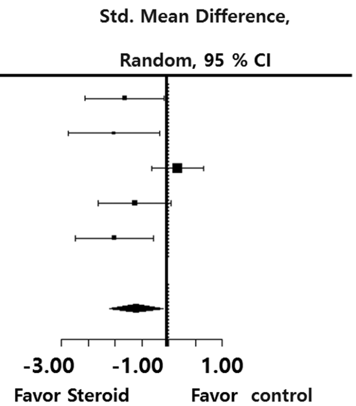

Figure 2. Preoperative administration of steroids versus placebo: standard mean difference of intraoperative bleeding (total: number of participants per group).

Study	Steroid total	control total	Weight	Std. Mean Difference, Random, 95 % CI
Fraire (2013)	14	17	19.4%	-0.71 [-1.44, 0.02]
Ecevit (2015)	10	12	15.1%	-1.45 [-2.39, -0.51]
Günel (2015)	33	32	25.9 %	-0.23 [-0.71, 0.25]
Sieskiewicz (2006)	18	18	20.7%	-0.76 [-1.44, -0.08]
Albu (2010)	17	16	18.8%	-1.47 [-2.23, -0.71]
Total (95 % CI)	**59**	**63**	**100 %**	**-0.85 [-1.34, -0.36]**

Heterogeneity : Q(df = 4) = 10.0810, *P* val = .0391, I^2 = 58.95%

Test for overall effect : Z = --3.4296 (*P* = .0006)

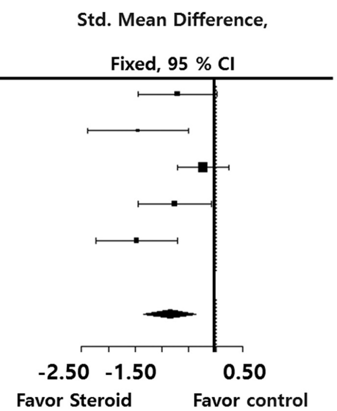

Figure 3. Preoperative administration of steroids versus placebo: standard mean difference of the visibility of the surgical field (total: number of participants per group).

Study	Steroid total	control total	Weight	Std. Mean Difference, Fixed, 95 % CI
Fraire (2013)	14	17	27.3 %	-0.44 [-1.15, 0.27]
Ecevit (2015)	10	12	19.2 %	-0.91 [-1.79, -0.03]
Sieskiewicz (2006)	18	18	29.1 %	-0.71 [-1.39, -0.03]
Albu (2010)	17	16	24.4 %	-1.42 [-2.18, -0.66]
Total (95 % CI)	**59**	**63**	**100 %**	**-0.85 [-1.26, -0.43]**

Heterogeneity : Q(df = 3) = 3.6387, *P* val = .3032, I^2 = 19.47 %

Test for overall effect : Z = -3.9882 (*P* <.0001)

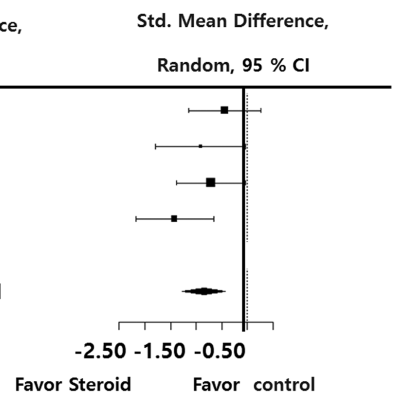

Figure 4. Preoperative administration of steroids versus placebo: standard mean difference of the operative time (total: number of participants per group).

Table 3. Subgroup Analysis of the Effects of Administration Type on Operative Bleeding, Operative Field Visibility, and Operation Time.

	Effect Size (95% CI), *P* Value		
	Operative Bleeding, mL	Operative Field Visibility[a]	Operation Time (Min)
Overall results	–0.60 (–1.09, –0.11), *P* = .0164	–0.85 (–1.32, –0.36), *P* = .0006	–0.84 (–1.26, –0.43), *P* < .0001
Systemic	–0.51 (–1.07, 0.05), *P* = .0747	–0.68 (–1.15, –0.21), *P* = .0042	–0.65 (–1.08, –0.23), *P* = .0025
Topic	–1.01 (–1.74, –0.28)	–1.47 (–2.23, –0.71)	–1.42 (–2.18, –0.66)

Abbreviation: 95% CI, 95% confidence interval.
[a]Scale assessed by clinicians.

complications, such as damage to the skull base or orbit.[8] Additionally, bleeding increases the operative time due to the need for multiple pauses during the surgery for suctioning and packing.[10,11] In particular, because increased inflammation and vascularity are usually observed in cases of chronic rhinosinusitis with polyps, increased intraoperative bleeding is expected in these cases, and a positive correlation has been observed between bleeding and primary ESS for polyps.[11]

During ESS, steroids inhibit damage to blood vessels, transudation formation, and tissue edema by decreasing mediators of the inflammatory process in the nose and sinus mucosa. Corticosteroids increase the spastic reactivity of the smooth muscles and heighten the effects of endogenous adrenaline and noradrenaline by affecting vascular constriction in microcirculation. Because of the traumatic effects of the endoscope and the surgical tools during surgery, the strong antiedematous effects of steroids are particularly important in the narrow areas of the nasal cavity.[8] To date, there have been several investigations into the efficacy of preoperative steroid administration in reducing intraoperative bleeding, including assessing the impact of different routes (systemically or locally) and various doses and schedules.[5-9] A literature review by Khosla et al pooled data from these studies in an attempt to derive a conclusion regarding the impact of steroids on intraoperative bleeding, surgical field visibility, and operative time associated with ESS in patients with nasal polyps.[3] However, this review enrolled only 2 studies due to a paucity of relevant work.[3] Although it is possible to conduct a meta-analysis with only 2 studies, the information gathered from more studies and subjects could lead to a more accurate estimation of the treatment effect and thus provide more powerful results.[12] Therefore, these authors suggested that further research needs to be conducted to investigate the beneficial properties of steroid therapy.[3]

Since the publication of that review, 3 additional studies have been published on the effects of preoperative steroids.[5-7] In this study, we had the benefit of these additional articles to maximize the data included in the meta-analysis. However, these studies assessed different steroids with various doses and schedules, and each ESS procedure could also be influenced by differences in the patient's inflammatory status and the surgeon's skill. These factors make it impossible to review the available studies with strict and narrow standardization. Although the various steroid preparations and doses have different pharmacokinetics, no significant differences have been found among preparations with regard to their effects on inflammation, edema, and intraoperative bleeding.[13,14] Khosla et al also considered different preparations, durations, and routes of steroids as 1 entity in their meta-analysis.[3] Therefore, this analysis included studies with wide standardization criteria (various preparation methods and steroid dosages before the ESS procedure). Additionally, we divided the enrolled studies into 2 subgroups based on systemic and topical administration to assess the separate effect sizes of these measurements.

Our results showed that intraoperative bleeding and operation time were both significantly reduced in the steroid group as compared with the control group. Moreover, surgical field visibility was significantly improved in the steroid group. The inhibitory effect of steroids in the local inflammatory process could explain the observation that preoperative steroid use appears to be a beneficial tool in improving ESS.[8] Our results indicate that the decreased intraoperative bleeding associated with preoperative steroid use is beneficial given the cleaner surgical field and shortened operative time.[3] The effect size for the assessments with respect to intraoperative bleeding, surgical field visibility, and operation time were >0.5, which indicated that these effects were clinically efficient during ESS.[15] In particular, the effect sizes for surgical field visibility and operation time were relatively larger than those for intraoperative bleeding.[15]

Additionally, subgroup analyses according to administration type were used to reduce the heterogeneity and to evaluate for other factors that could influence the results. The use of steroids had a significant effect on surgical field visibility and operation time, regardless of administration type. However, although the blood loss in the systemic and topical subgroups was significantly reduced when compared with the control and even though the effect sizes in both subgroups were >0.5, the effect size in the systemic subgroup was significantly lower versus the topical subgroup. These results could show that the effect size of preoperative systemic steroids seemed to be lower than that of topical steroids; however, among total 5 enrolled studies, 4 studies evaluated the effect of systemic steroid administration. By contrast, only a single study by Albu et al assessed the effect of topical steroid.[9] There was a definite difference in sample size between the oral and topical steroid groups, which would make it difficult to evaluate the comparative advantage of individual treatment directly based on simply effect size of each treatment. Additionally, given that combining the results of more studies into 1 large study could allow for a more precise estimate of the true effect size, the results for systemic steroid administration would reflect a true effect more accurately. Therefore, it could be commented that the administration type would be a factor to influence the results without the mention regarding good or bad of a certain method. Enrolling more studies regarding the effect of topical steroid needs be performed in the future to judge the separate topical steroid effect exactly.

Although the quantification of blood loss and the assessment of the endoscopic visibility of the surgical field have been used to evaluate the effects of bleeding during ESS, 1 critique has been that the measurement of blood loss from suctioned contents is inaccurate, as rinsing fluids are collected in the suction bottles along with saline, tissue, and blood. In contrast, subjective grading of the surgical field is easy to use, is a more dynamic measurement tool, and can be repeated multiple times during the procedure in response to surgical maneuvers.[9] The operative time is also an important measurement tool for blood loss during ESS.[3] Given these mentions in the literature, we could argue that surgical field visibility and operative time should hold greater importance. Our study found significant evidence that preoperative steroids are effective in reducing blood loss in ESS, regardless of the type of administration.

However, the use of steroids is not always harmless. Corticosteroids elicit metabolic changes in a variety of biochemical components and suppress immune and inflammatory responses and functions of the central nervous system.[16,17] It is important to balance the benefits of steroid treatment with the potential for side effects, especially with high-dose systemic therapy.[4] When corticosteroids are used with short-term hypothalamic-pituitary-adrenal axis suppression, hyperglycemia, gastrointestinal effects, and psychiatric effects would occur as complications. Also, avascular necrosis of the femoral head, osteoporosis, cushingoid appearance, accelerated atherosclerosis, early cataracts, and skin thinning and purpura are known to be associated with chronic corticosteroid, although these are unlikely to occur at dosage regimens used in otolaryngology.[4] In this meta-analysis, the side effects related to steroids were reported in only 1 study regarding topical administration, and meta-analysis was not possible.[9] Although there was no single criterion on the duration and dosage of systemic steroids in the enrolled studies, they were administered in doses that ranged from 30 to 60 mg/d within 7 days, with or without tapering.[5-8] These duration and dose of steroids may cause minimal adverse effects of preoperative systemic steroids. However, this study had a limitation in terms of measurement—namely, that the adverse effects of oral steroid administration were not reported quantitatively or concretely in the enrolled studies. Clinicians should pay attention to the possible adverse effects of systemic steroids. Based on our results, the preoperative administration of steroids could alleviate intraoperative bleeding without significant adverse effects in patients with nasal polyps who are undergoing ESS. However, with the relatively small number of studies that were included, additional clinical trials are needed to confirm the results of this study and to establish preoperative guidelines.

Conclusion

This study demonstrated that the preoperative administration of steroids in patients with nasal polyps could effectively reduce intraoperative bleeding, decrease operation time, and improve the visibility of the surgical field during ESS. However, treatment duration and dosing standard require further investigation, and more trials need to be included.

Author Contributions

Se Hwan Hwang, study conception and design, acquisition of data, analysis and interpretation of data, drafting the article and revisions, final approval of article; **Jae Hyun Seo,** acquisition of data, analysis and interpretation of data, drafting the article and revisions, final approval of article; **Young Hoon Joo,** study conception and design, analysis and interpretation of data, drafting the article and revisions, final approval of article; **Jun Myung Kang,** study conception and design, acquisition of data, analysis and interpretation of data, drafting the article and revisions, final approval of article.

Disclosures

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