# Effect of intraoperative injection of 0.25% bupivacaine with 1:200,000 epinephrine on intraoperative blood loss in FESS

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## ABSTRACT

**Background:** *This study was designed to compare differences in intraoperative blood loss, mean arterial blood pressure (MABP), and duration of surgery when 0.25% bupivacaine with 1:200000 epinephrine is injected, preoperatively, versus normal saline (NS), during functional endoscopic sinus surgery (FESS).*

**Methods:** *A prospective, double-blind randomized placebo-controlled study was performed. Part I involved 46 patients who were infiltrated with 0.25% bupivacaine with 1:200000 epinephrine on one side of the nose and sterile NS on the other (control). Part II involved 30 patients infiltrated with 0.25% bupivacaine with 1:200000 epinephrine bilaterally and 30 patients with NS bilaterally (control). Patient demographics, preoperative MABP, intraoperative MABP, duration of surgery, and total estimated blood loss (EBL) were recorded for each side (part I) and case (part II).*

**Results:** *For part I, there were 46 patients (mean age, 49 years), 24 women and 22 men. MABP was 72 mmHg for each side ($p = 0.97$). Preoperative MABP was 93 mmHg. Duration of surgery was 48 minutes for epinephrine side and 45 minutes for control ($p = 0.17$). Total EBL was 185 mL for the epinephrine side and 197 mL for control ($p = 0.53$). For part II, there were 60 patients (mean age, 56 years), 28 women and 32 men. The MABP was 77 mmHg for the epinephrine group and 72 mmHg for control ($p = 0.048$). Preoperative MABP was 100 mmHg for the epinephrine group and 97 mmHg for control ($p = 0.37$). Duration of surgery was 2.25 hours for the epinephrine group and 2.08 hours for control ($p = 0.17$). Total EBL was 589 mL for the epinephrine group and 538 mL for control ($p = 0.64$).*

**Conclusion:** *There was no significant reduction in intraoperative blood loss during FESS when local anesthetic containing epinephrine was used compared with infiltration with NS. More importantly, part II shows a significantly higher MABP associated with infiltration of epinephrine. Parts I and II did not show a significant difference in preoperative MABP or duration of surgery.*

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**Key words:** Blood loss, epinephrine, FESS, functional endoscopic sinus surgery, hemostasis, infiltration, injection, MABP, normal saline

Functional endoscopic sinus surgery (FESS) of the paranasal sinuses has become widely accepted as the treatment of choice for patients with chronic rhinosinusitis. Because of the highly vascularized nature of the nasal cavity and the restricted confines of the middle meatus, intraoperative bleeding can become a major hindrance during FESS. It is of principal importance for the sinus surgeon to maintain an optimal endoscopic field of vision because an obstructed view secondary to bleeding can lead to potentially poor surgical outcomes. A correlation has been identified between blood loss and surgical field visualization.[1] At our institution, several techniques are used to decrease nasal congestion and minimize intraoperative bleeding. All patients undergoing FESS receive corticosteroid and antibiotics for 7 days before surgery, xylometazoline nasal spray and packing for decongestion immediately preoperatively, and intraoperative infiltration of the lateral nasal wall with 0.25% bupivacaine with 1:200,000 epinephrine. These hemostatic measures are standard procedure at our institution for all patients undergoing FESS. Some investigators have found total i.v. anesthesia as a useful method of reducing blood loss and have shown an improvement over conventional anesthesia during FESS.[2,3] Despite these techniques, blood loss continues to pose difficulties during sinus surgery.

In addition, the potential for complications related to the use of epinephrine must always be considered because its systemic absorption can lead to major complications for the patient. The toxicity of epinephrine is directly related to its concentration in the blood. Epinephrine-related side effects include hypertension, hypotension, tachycardia, bradycardia, and other serious arrhythmias. Despite possible complications and minimal evidence supporting intraoperative infiltration with epinephrine, current FESS standards continue to advocate for this technique. The potential for complications related to infiltration with local anesthetics was also a motivating factor for this study. Systemic absorption of local anesthetic has well-documented side effects, which directly correlate with serum levels. Therefore by limiting the use of both local anesthetic and epinephrine, one can further optimize patient safety during FESS.

The purpose of this study was to compare differences in intraoperative blood loss, mean arterial blood pressure (MABP), and surgical time when 0.25% bupivacaine with 1:200,000 epinephrine was injected during FESS compared with the infiltration of sterile normal saline (NS). We hypothesized that the infiltration of the lateral nasal wall with local anesthetics and epinephrine offers no advantage with respect to the amount of blood loss during FESS.

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## MATERIALS AND METHODS

Institutional Clinical Research Ethics Board approval was obtained for the study. Informed consent was also obtained from all study subjects. A prospective, randomized, double-blinded study was performed.

This study was divided into two parts in an effort to confirm the proposed hypothesis. Forty-six patients were included in part I of the study, and sixty patients undergoing bilateral FESS were enrolled in part II. Patients undergoing surgery for chronic rhinosinusitis, either revision or primary surgery, were eligible for enrollment. Patients undergoing unilateral FESS, surgery for tumor resection, or allergic fungal sinusitis, or those allergic to bupivacaine were excluded from this study. In addition, excluded were those patients with incomparable disease severity on each side of the nose. The Lund-Mackay (L-M) CT scoring system to assess severity of mucosal disease was used for this purpose; an L-M score difference of less than $\pm 2$ between the two sides was necessary for enrollment. There were no attempts made to grade the surgical field intraoperatively.

The initial protocol for part I involved using lidocaine 1% with 1:100,000 epinephrine. This was changed to 0.25% bupivacaine with 1:200,000 epinephrine after several patients experienced hypertensive episodes, with one patient developing ST segment depression as seen on intraoperative electrocardiogram. These patients were excluded from the study, and the project was restarted with the updated protocol.

All patients were treated with antibiotics and corticosteroids for 7 days preoperatively and received CT imaging as per standard protocol. Imaging was performed at various times before the date of surgery and not recorded as part of the analysis. Preoperative MABP was measured for each patient before surgery. The allocation of type of injection (saline versus epinephrine) for each side (part I) and for each patient (part II) was decided randomly by coin toss with the primary surgeon unaware of this assignment. The scrub nurse and anesthesiologist were aware of patient assignment. The scrub nurse was responsible for preparing the intraoperative injections. ~2–3 mL of anesthetic or placebo was injected at the anterior buttress of the middle turbinate on each side. A blanching effect was seen with both injections thereby allowing the surgeon to remain blinded. Intraoperative blood loss was calculated by the circulating nursing staff who were blinded to the injection sides. In part I, the blood loss from each side was contained separately and contamination from the other side was avoided. After surgical completion of the first side in each case, a neuropattie was placed in the paranasal sinuses. A Merocel sponge (Medtronic, Jacksonville, FL) was placed in the nasopharynx at the beginning of every case, creating a physical barrier between the two sides. This allowed for calculated blood loss to be free of cross-contamination from the first side as the operation proceeded. Under a general anesthetic, a single sinus surgeon performed all surgeries. There were no specific attempts made by the anesthesiologist to control the MABP in part I or II. However, in all cases the anesthesiologists were asked to maintain a systolic blood pressure of $<100$ mmHg. Anesthetic parameters, including end-tidal $CO_2$ and percentage of inhalational agents, were kept relatively constant and were not recorded or compared in this study.

### Part I

Two separate 10-mL syringes were prepared. One syringe contained 0.25% bupivacaine with 1:200,000 epinephrine, and the second syringe contained sterile injectable NS (placebo). Each subject acted as their own control, with the contralateral side being injected with placebo. Surgery was performed as routine. Patient demographics, preoperative MABP, intraoperative MABP, and duration of surgery were recorded for each side. At the conclusion of surgery on each side, blood loss was meticulously calculated by adding all of the suctioned fluid from the surgical field and subtracting the amount of irrigation used during the case.

### Part II

The measures taken for preoperative, intraoperative, and postoperative management were identical to those in part I. Subjects in this part were divided into two groups. One group received infiltration with 0.25% bupivacaine with 1:200,000 epinephrine bilaterally. The other group received infiltration with sterile NS (placebo) bilaterally. Once again, the operating surgeon was blinded to the solution used for infiltration. Patient demographics, preoperative MABP, intraoperative MABP, duration of surgery, and blood loss were measured for each case.

Statistical analysis of all data reported in this study was performed using SPSS 16.0 (SPSS, Inc., Chicago, IL). A parametric paired Student's *t*-test was used to assess the difference between the means for estimated blood loss, MABP, and total surgical time. To ensure disease comparability between sides for each patient, a nonparametric Wilcoxon signed rank test was used to test the difference of the means of L-M scores.

## RESULTS

### Part I

*Patient Demographics.* Forty-six patients were enrolled. The mean age was 49 years old (range, 15–73 years). There were 24 women (52%) and 22 men (48%; Table 1).

### Part II

*Patient Demographics.* Sixty patients were enrolled. The mean age was 56 years old (range, 23–84 years). There were 28 women (47%) and 32 men (53%; Table 2).

## DISCUSSION

### Part I

In part 1 of the study, injection of local anesthetic with epinephrine did not result in a reduction in blood loss. With all patient factors being similar (preoperative MABP, patient age, and L-M score), neither intraoperative MABP nor duration of surgery showed any statistically significant difference between the two groups.

### Part II

In part 2 of the study, injection of local anesthetic with epinephrine did not result in a reduction in blood loss. Interestingly, our results showed a significantly higher in-

Table 1 **Injection study: Part I**

| | Injection | Mean | *p*Value |
|---|---|---|---|
| Patient age (yr) | N/A | 49.4 | N/A |
| L-M score | NS | 7.28 | 0.62* |
| | Epinephrine | 7.24 | |
| Preoperative MABP (mmHg) | N/A | 92.87 | N/A |
| Surgical time (min) | NS | 44.78 | 0.17# |
| | Epinephrine | 48.11 | |
| Intraoperative MABP (mmHg) | NS | 72.15 | 0.97# |
| | Epinephrine | 72.11 | |
| EBL (mL) | NS | 184.90 | 0.53# |
| | Epinephrine | 196.09 | |

**Wilcoxon signed ranks test.*
*#Independent sample Student's t-test.*
*NS = normal saline; epinephrine = local anesthetic containing epinephrine; EBL = estimated blood loss; MABP = mean arterial blood pressure.*

Table 2 **Injection study: Part II**

| | Injection | Mean | *p* Value |
|---|---|---|---|
| Patient age (yr) | NS | 57.2 | 0.41# |
| | Epinephrine | 54.5 | |
| L-M score | NS | 7.37 | 0.65* |
| | Epinephrine | 7.88 | |
| Preoperative MABP (mmHg) | NS | 97.19 | 0.37# |
| | Epinephrine | 100.32 | |
| Surgical time (min) | NS | 2.23 | 0.19# |
| | Epinephrine | 2.36 | |
| Intraoperative MABP (mmHg) | NS | 72.23 | 0.48# |
| | Epinephrine | 77.07 | |
| EBL (mL) | NS | 538.67 | 0.636# |
| | Epinephrine | 589.17 | |

**Wilcoxon signed ranks test.*
*#Independent sample Student's t-test.*
*NS = normal saline; epinephrine = local anesthetic containing epinephrine; EBL = estimated blood loss; MABP = mean arterial blood pressure.*



traoperative MABP in the epinephrine group compared with the control group ($p = 0.048$). There was no statistically significant difference in preoperative MABP, duration of surgery, patient age, or L-M scores between the two groups.

Several previous studies have explored varying concentrations of epinephrine used together with local anesthetic with the goal of reducing intraoperative blood loss. Gessler *et al.* found no significant difference in blood loss during ear surgery when various concentrations were used.[4] Studies by O'Malley *et al.* and Dunlevy *et al.* also noted no significant advantage to higher concentrations of epinephrine.[5,6] Temple *et al.* found no benefit in blood loss reduction during laser turbinectomy when comparing 2% lidocaine with 1:80000 epinephrine versus saline.[7] Similarly, Vanniasegaram found no advantage in using epinephrine during septal surgery.[8] Wormald *et al.* found a significant improvement in the surgical field when the pterygopalatine fossa was infiltrated with epinephrine; however, total blood loss was not evaluated.[9] The current study used local anesthetic (bupivacaine) with 1:200,000 epinephrine in 106 patients (both parts 1 and 2), and no significant advantage with respect to blood loss was identified in the epinephrine group.

The potential for epinephrine-related complications was a significant motivating factor for performing this study. There were no complications related to the use of epinephrine contained in local anesthetic in this study. However, systemic absorption remains a practical concern during FESS. Epinephrine is a potent agent that can result in systemic toxicities of varying magnitude; examples of such side effects include hypertension, hypotension, tachycardia, bradycardia,

and other arrhythmias.[10] This is of particular concern when cocaine on cotton pledgets is used to pack the nose preoperatively. Cocaine potentiates the injected epinephrine, increasing the possibility of toxic side effects.[11] Anderhuber *et al.* found that even though systemic absorption of locally injected vasoconstrictors occur, adrenalin-related side effects during FESS are extremely rare when the patient is in a monitored setting.[12] Several other studies have described alteration of hemodynamic states after the injection of local anesthetic containing epinephrine.[2,13] Generally, the use of epinephrine in local anesthetic is safe practice; however, close monitoring of the patient is necessary to prevent serious complications.

Preoperative preparation is important in decreasing blood loss and improving visualization in the surgical field. Nair *et al.* suggested an improved surgical field when patients were premedicated with β-blockers [14] Sieskiewicz *et al.* noted a significantly better surgical field when patients were premedicated with corticosteroids, even though the total blood loss was only minimally reduced in the steroid group.[15] Shi *et al.* also showed reduced bleeding during FESS when preoperative inflammation was controlled in patients with chronic sinusitis and nasal polyposis [16] A reduction in blood loss should theoretically result in improved surgical visualization and shorter duration of surgical time. At our institution, patients are premedicated with antibiotics and corticosteroids to prime the surgical field for surgery by decreasing active infection and mucosal inflammation, with an associated anticipation of a reduction in blood loss.

Various anesthetic techniques have also been trialed and recommended with the aim to minimize surgical blood loss. It is believed that capillary bleeding, affected by an elevated MABP, is the key factor causing increased surgical blood loss.[17] Cincikas *et al.* and Saitoh *et al.* showed reduced intraoperative bleeding and improved surgical field with controlled hypotension.[1] However, several studies have showed little correlation between MABP and surgical blood loss.[17–20] Wormald *et al.* indicated that surgical field visualization was not always improved as a consequence of reducing MABP. This may be a result of the side effects of the pharmaceutical agent being used, *i.e.*, rebound hypertension, reflex tachycardia, vasodilation, and myocardial depression.[3] Because maintaining a hypotensive state has not always been found to improve surgical field on its own, Nair *et al.* have shown that preadministration of β-blockers to induce bradycardia has shown to improve the surgical field.[14] Total i.v. anesthesia has also been investigated as a means of minimizing blood loss, and has showed an improvement over conventional anesthesia during FESS.[3,21]

## CONCLUSION

There is no significant reduction in intraoperative blood loss during FESS when local anesthetic containing epinephrine is used compared with infiltration with NS. More importantly, results from the second part of our study indicate that there was a significantly higher intraoperative MABP associated with the infiltration of epinephrine when compared with the use of NS. Every attempt should be made to improve the surgical field and minimize blood loss by adequately preparing the patient preoperatively. Maintaining a safe level of controlled hypotension and bradycardia has proven to be important intraoperative factors in improving surgical field visualization.

## REFERENCES


1. Cincikas D, and Ivaskevicius J. Application of controlled arterial hypotension in endoscopic rhinosurgery. Medicina 39:852–859, 2003.
2. Yang JJ, Li WY, Jil Q, et al. Local anesthesia for functional endoscopic sinus surgery employing small volumes of epinephrine-containing solutions of lidocaine produces profound hypotension. Acta Anaesthesiol Scand 49:1471–1476, 2005.
3. Wormald PJ, van Renen G, Perks J, et al. The effect of the total intravenous anesthesia compared with inhalational anesthesia on the surgical field during endoscopic sinus surgery. Am J Rhinol 19:514–520, 2005.
4. Gessler E, Hart K, Dunlevy T, and Greinwald J. Optimal concentration of epinephrine for vasoconstriction in ear surgery. Laryngoscope 111:1687–1690, 2001.
5. O'Malley TP, Postma GN, Holtel M, et al. Effect of local epinephrine on cutaneous blood flow in the human neck. Laryngoscope 105:140–143, 1995.
6. Dunlevy TM, O'Malley TP, and Postma GN. Optimal concentration of epinephrine for vasoconstriction in neck surgery. Laryngoscope 106:1412–1414, 1996.
7. Temple RH, and Timms MS. Blood loss reduction during laser turbinectomy. Rhinology 39:230–232, 2001.
8. Vanniasegaram I. Prospective study of the use of vasoconstrictor and saline in septal surgery for infiltration. J Laryngol Otol 105:638–639, 1991.
9. Wormald PJ, Athanasiadis T, Rees G, and Robinson S. An evaluation of effect of pterygopalatine fossa injection with local anesthetic and adrenalin in the control of nasal bleeding during endoscopic sinus surgery. Am J Rhinol 19:288–292, 2005.
10. Yang JJ, Yang QP, Wang TY, et al. Marked hypotension induced by adrenaline contained in local anesthetic. Laryngoscope 115:348–352, 2005.
11. Wang SH, Wang HW, and Wang JY. Effects of cocaine on human nasal mucosa. Eur Arch Otorhinolaryngol 250:245–248, 1993.
12. Anderhuber W, Walch C, Nemeth E, et al. Plasma adrenaline concentrations during functional endoscopic sinus surgery. Laryngoscope 109:204–207, 1999.
13. Zhao F, Wang Z, Yang SJ, et al. Low-dosage adrenaline induces transient marked decrease of blood pressure during functional endoscopic sinus surgery. Am J Rhinol 20:182–185, 2006.
14. Nair S, Collins M, Hung P, et al. The effect of B-blocker premedication on the surgical field during endoscopic sinus surgery. Laryngoscope 114:1042–1046, 2004.
15. Sieskiewicz A, Olszewska E, Rogowski M, and Grycz E. Preoperative corticosteroid oral therapy and intraoperative bleeding furing functional endoscopic sinus surgery in patients with severe nasal polyposis: A preliminary investigation. Ann Otol Rhinol Laryngol 115:490–494, 2006.
16. Shi JB, Yang QT, Wen WP, and Xu G. Study of bleeding during surgery for chronic sinusitis and nasal polyp influenced by preoperative treatment. Zhonghua Er Bi Yan Hou Ke Za Zhi 38:202–205, 2003.
17. Jacobi K, Bohm B, Rickauer A, et al. Moderate controlled hypotension with sodium nitroprusside does not improve

surgical conditions or decrease blood loss in endoscopic sinus surgery. J Clin Anesth 12:202–207, 2000.
18. Schindler I, Andel H, Leber J, and Kimla T. Moderate induced hypotension provides satisfactory operating conditions in maxillofacial surgery. Acta Anaesthesiol Scand 38:384–287, 1994.
19. Fromme GA, MacKenzie RA, Gould AB Jr, et al. Controlled hypotension for orthognathic surgery. Anesth Analg 65:683–686, 1986.
20. Eltringham RJ, Young PN, Fairbairn ML, and Robinson JM. Hypotensive anaesthesia for microsurgery of the middle ear. A comparison between enflurane and halothane. Anaesthesia 37:1028–1032, 1982.
21. Eberhart LH, Folz BJ, Wulf H, and Geldner G. Intravenous anesthesia provides optimal surgical conditions during microscopic and endoscopic sinus surgery. Laryngoscope 113: 1369–1373, 2003. □