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Comparison of Cardiac Indices Using Two Different Concentrations of Topical Adrenaline during Endoscopic Transsphenoidal Pituitary Surgery: A Prospective Randomized Observational Study

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Abstract

Introduction Adrenaline-soaked wicks are often employed to decongest nasal mucosa during transsphenoidal pituitary surgeries to ensure proper hemostasis and visibility of the operating field. Considerable debate exists regarding the optimum concentration of adrenaline that strikes a balance between hemostasis as well as the hemodynamic side effects of adrenaline. This study assessed cardiac indices like cardiac output and cardiac index using a FloTrac Vigileo cardiac output monitor to compare two different concentrations of adrenaline used for topical instillation.

Methods and Materials 60 adult patients undergoing transsphenoidal pituitary surgery were randomly assigned to receive cotton wicks soaked in adrenaline solution (either 1:100,000 or 1:200,000) for nasal decongestion. Following a standardized anesthetic regime, a FloTrac Vigileo cardiac output monitor was attached with the invasive arterial line for precise monitoring and recording of cardiac indices (cardiac output and cardiac index). Additionally, quality of surgical field (as reported by the operating surgeon) blood loss, incidences of adverse hemodynamic events, and rescue drug usage were recorded.

Results No difference in cardiac outputs and cardiac indexes of the patients was observed during baseline to 55 minutes and at 80 minutes and onward, whereas difference rose to statistical significance at the time points of 60 minutes and 70 minutes ($p < 0.05$). Other parameters like stroke volume, stroke volume variation, and hemodynamic parameters were similar. Quality of the surgical fields (as reported

Keywords
- blood pressure
- catecholamine
- epinephrine
- hemostasis
- pituitary
- vasoconstriction

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by the surgeon), intraoperative bleeding, incidences of adverse effects, and frequency of rescue drugs usage were similar.

Conclusion Instillation of 1:100,000 dilution of adrenaline solution compared with 1:200,000 for nasal decongestion is associated with significant rise in cardiac output and cardiac index at 60 and 70 minutes of the surgery with similar blood loss and hemodynamic variables. Therefore, the lower concentration of adrenaline can be recommended for usage during transsphenoidal pituitary surgeries.

Introduction

Endoscopic transsphenoidal pituitary surgery (ETSS) is the standardized and commonly performed surgical technique for the treatment of pituitary tumors.[1] The nasal mucosa, especially of the inferior turbinates, being extremely vascular is prone to oozing, which can considerably impair the view of the surgical field leading to prolonged operative times, incomplete surgical interventions, difficulty in identifying landmarks, and injury of important anatomical structures.[2,3] Various strategies to reduce bleeding during ETSS include head elevation, hypotensive anesthesia, total intravenous (IV) anesthetics, injecting or topical usage of vasoconstrictive drugs such as cocaine, oxymetazoline, and adrenaline.[4] Adrenaline functions as a capillary vasoconstrictor, and being inexpensive and easily available it is commonly used intranasally (either as submucosal injection or topical mucosal application) during ETSS.[5] Systemic absorption of adrenaline can cause hypertension and tachycardia secondary to raised cardiac output (CO). The elevated CO can be counterproductive as it can increase surgical site bleeding thereby obscuring the field. There is lack of consensus on the exact dosage of adrenaline that should be used in ETSS and diverse concentrations ranging from 1:200,000 to 1:1000 topically and 1:200,000 to 1:50,000 for infiltration have been used.[6] Various techniques have been developed to determine the CO using the arterial wave form. Among them, the FloTrac system (Edwards VigileoTM system; Edwards Lifesciences, Irvine, California, United States) uses the FloTracTM sensor connected to arterial pressure tubing, does not require calibration, and provides continuous CO measurements from the arterial pressure wave[7] (►**Fig. 1**). Additionally, cardiac index (CI), stroke volume (SV), stroke volume variation (SVV), and stroke volume index (SVI) are some of the other values that can also be derived by the analysis of arterial wave forms.

Fig. 1 FloTrac device.

In our institute, traditionally 1:100,000 dilution of adrenaline was used topically for vasoconstriction in ETSS. We hypothesized that lowering the concentration of adrenaline to 1:200,000 will provide lesser increase of CO and better preservation of hemodynamic parameters measured sensitively using a FloTrac device without compromising hemostasis and quality of the surgical field.

We, therefore, designed and undertook this randomized prospective comparative study to compare two different concentrations—1 mg/mL saline (1:100,000) and 0.5 mg/mL in 100 mL saline (1:200,000) of nasal adrenaline instillation on the hemodynamic profiles and CIs obtained from FloTrac device during ETSS for pituitary adenomas under general anesthesia as the primary objective. Secondary objectives were to compare the quality of surgical field, blood loss, and adverse effects encountered.

Materials and Methods

Following approval from the Institute Ethics Committee (2020-14-MD-114 dated 17 February 2020) and subsequent to registering the trial with the Clinical Trial Registry of India (CTRI/2020/03/024374 [Registered on: 31/03/2020]), and obtaining written and informed consent from eligible patients, 62 eligible patients who were undergoing ETSS for pituitary adenoma under general anesthesia were enrolled in this prospective randomized patients and data analysis blinded, parallel group study using consecutive sampling (►**Fig. 2**). The study was conducted between 20/07/2020 and 14/07/2021 in the neurosurgery operation theaters of Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India. Enrolled patients were given the option to withdraw themselves from the study at any moment without stating any reason. Patients (18–65 years) of either gender belonging to American Society of Anesthesiologists physical status I or II and who were undergoing transsphenoidal surgery for pituitary adenomas were eligible for inclusion. Patients who were unable (legally incompetent) or unwilling to give consent, patients with decreased level of consciousness, raised intracranial tension, recurrent pituitary tumor, and pituitary apoplexy; patients with any cardiac pathology, severe hypertension, or previous nasal surgery; patients with history of allergy to any of the study drugs; and patients of body weight less than 40 kg were excluded from the study.

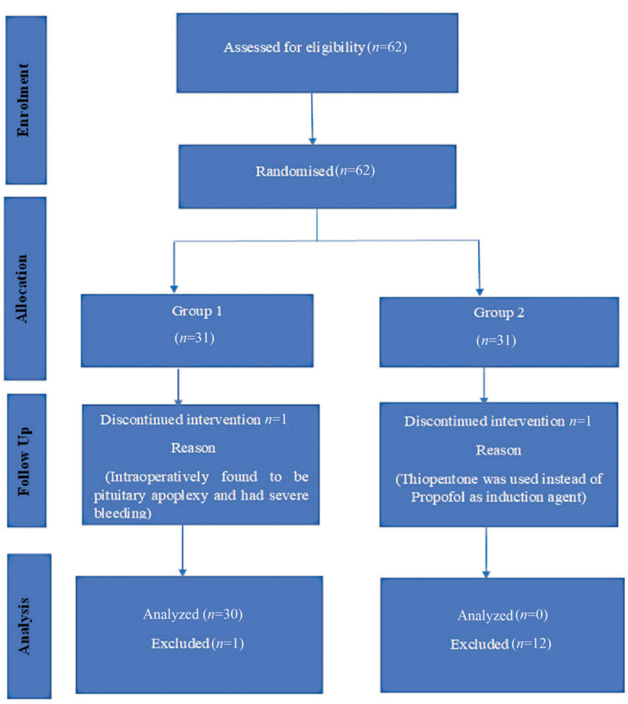

Fig. 2 Consolidated Standards of Reporting Trials (CONSORT) statement.

Sample size was calculated based on a pilot study conducted on five patients in each group where COs were compared. CO in group 1 (0.5 mg) and group 2 (1 mg) obtained were 4.05 ± 0.15 and 4.16 ± 0.13, respectively (effect size between means = 0.784). At minimum two-sided 95% confidence interval and 80% power of the study, minimum required sample size in group 1 and group 2 came out to be 27. Finally in this study, we included 30 patients in each group to account for study errors or attrition. Sample size was estimated using software G Power version—3.1.9.2 (Düsseldorf University, Germany). Based on a computer-generated sequence of randomization (obtained from http://www.randomization.com), a 1:1 group allocation was done and was kept concealed in opaque sealed envelopes.

All the eligible participants were briefed about the study protocol, its potential harm, and benefits. Only the willing patients were recruited after obtaining written and informed consent in English or Hindi 1 day prior to surgery stating their willingness to be included in the study. They were informed categorically that they can withdraw themselves from the study at any time without stating any reason. The research participants were treated with highest ethical standards as per the Declaration of Helsinki.

On the night before surgery, during their preanesthetic check-up, the eligible patients were apprised of their inclusion in the trial and explained in detail the manner of conducting the study. Their detailed history, examination, and routine preoperative investigations were again reviewed.

All patients were premedicated with tablet alprazolam 0.04 mg/kg and tablet ranitidine 150 mg the night before and 2 hours before surgery. On the day of surgery, upon arrival to the operation theater, IV access was achieved with 16 or 18 G IV cannula under local anesthesia with 2% lignocaine. Five-lead-electrocardiogram, noninvasive blood pressure (NIBP), and pulse oximetry were attached. Under local anesthetic infiltration, a 22G arterial cannula was placed in the radial artery of the nondominant hand and the FloTrac Vigileo monitor system (Edwards Lifesciences, Irvine, California, United States) was connected to the cannula and baseline data (age, weight, and height) were entered to calibrate the machine. Baseline values of CO, CI, SVV, SV and IBP were recorded.

Following preoxygenation with 100% oxygen for 3 to 5 minutes, induction of anesthesia was performed with titrated doses of midazolam (0.05–0.15 mg/kg IV), fentanyl (1–2 µg/kg IV), and 2% propofol (20 mg/mL) (1–2.5 mg/kg IV). Following administration of IV vecuronium (0.08–0.1 mg/kg

IV), the patients' trachea was intubated with appropriate-sized polyvinyl chloride cuffed endotracheal tube. Additional monitoring comprising of capnography (ETCO2), nasopharyngeal temperature, bispectral index (BIS), train of four (TOF), and Foley's catheter for urine output were attached. Anesthesia was maintained using oxygen, air (50% each), and sevoflurane 0.6 to 2.4% (inspired) started immediately after induction. Muscle relaxation was maintained by vecuronium infusion at 0.0008 to 0.001 mg/kg. Posterior pharyngeal packing was done with moist cotton gauze to avoid entry of the surgical bleeding to trickle into the esophagus.

Based on random number tables generated through computer program, sequentially numbered sealed envelopes containing the randomization codes were prepared beforehand for allotment of patients in two different groups. These sealed envelopes were now opened by the scrub nurse (not involved in the outcome assessment) before laying the surgical trolley and based on the codes either of the two different concentrations of adrenaline solution for instillation in the two groups were prepared and laid on the trolley for nasal instillation using cotton strips.

Group 1: adrenaline (0.5 mg/mL) diluted in 100 mL normal saline (1:200,000)

Group 2: adrenaline (1 mg/mL) diluted in 100 mL normal saline (1:100,000)

The concentrations were not divulged to the anesthesiologist and the surgeon. Cotton strips were now dipped in the solution to absorb it fully and then the excess solution was carefully squeezed until the cotton strip was saturated but not dripping even upon compression. Removal of the excess solution was done over the solution to avoid waste. After sterile painting and draping, cotton strips were then inserted in the nasal fossae (one each side), using nasal speculum and this procedure of nasal mucosal preparation continued for 10 to 15 minutes. Thereby, patients in group 1 received 1:200,000 adrenaline solution, whereas those in group 2 received 1:100,000 adrenaline solution in the nasal cavity by the operating surgeon. Patients were now placed in supine with slight head raised and tilted position. After approximately 10 to 15 minutes of repeated packing and removal of cotton strips soaked in adrenaline solution, which allowed for the drug to be absorbed, surgery commenced. Hemodynamic parameters and CIs were continuously recorded every 5 minutes for the first 1 hour and thereafter at every 10 minutes interval till the end of surgery by the single anesthesiologist who conducted all the cases and was blinded to the group allocation. All the patients were monitored using BIS that was targeted to be maintained between 40 and 60 throughout the operative procedure. TOF was kept less than 2 throughout the surgery. Normocapnia was maintained (35–40 mm Hg) by adjustment of ventilatory parameters and normothermia (35.5–36.5°C) was maintained with warming blankets, covering the exposed parts of the body and warm saline infusions. Intraoperative fluid administration was guided by the hourly maintenance requirements and losses and was done with 0.9% normal saline. The hemodynamic parameters were targeted to be maintained within 20% of the baseline values and the intraoperative management was done at the discretion of the attending anesthesiologist. In case of persistent mean arterial pressure (MAP) more than 25% of the preinduction baseline values and/or heart rate more than 90 bpm suggestive of inadequate analgesia, initially 0.5 µg/kg of fentanyl was administered. This was followed by injection metoprolol in intermittent dose of 1 mg/dose. If blood pressure could not be controlled with metoprolol injection, injection labetalol 5 to 10 mg bolus every 5 minute (maximum 200 mg) was administered. Lastly esmolol was considered with a loading dose of 500 µg/kg over 1 minute and maintenance dose of 50 to 100 µg/kg/minute over 4 minutes was used for controlling the blood pressure. In case of hypotension (MAP < 25%) of baseline, correction was first attempted with fluid bolus (100 mL) and if unresponsive, then with injection mephentermine 6 mg bolus. Treatment of bradycardia (heart rate <40/min) with atropine (0.6 mg IV) and of arrythmias as per Advanced Cardiac Life Support (ACLS) protocol was also planned. Usage of rescue drugs was also recorded

At the completion of surgery, the blood content in the suction canister and the blood soaked in the gauze strips were measured. The volume of blood in the suction canister was calculated by subtracting the irrigation saline used during the procedure and the volume of blood soaked in cotton strips was calculated by counting the strips that were partially or completely soaked with blood.

The single operating surgeon, who was blinded to the patient group allocation, evaluated the surgical field quality using the Boezaart scale[8] and graded it. It included five grades with grade 0 being no bleeding, grade 1 stated slight bleeding where no suction was required, grade 2 included slight bleeding and occasional suction was required, grade 3 also included slight bleeding but frequent suctioning was required, grade 4 defined moderate bleeding where frequent suctioning was needed, and surgical field was threatened and grade 5 includes severe bleeding that required constant suctioning and surgical field was threatened to such an extent where surgery could not be possible due to flooding of surgical field view.

At the end of surgery, sevoflurane was discontinued and muscle relaxation was reversed on obtaining a TOF count of 3. Oral throat pack was removed. All the patients were extubated inside the operation theater when the extubation criteria were met. The patients were then transferred to the post-anesthesia care unit for further care and monitoring from where they were shifted out once the transfer criteria were fulfilled (Aldrete score ≥9).

Results

In this study, a total of 62 patients were enrolled, of which 60 patients were analyzed. Analysis of baseline characteristics (age, weight, height, body mass index, duration of anesthesia and surgery, and blood loss) revealed no significant difference between the study groups for the patients ($p < 0.05$; ►**Table 1**). Comparison of the CIs revealed that there was no difference in COs and CI of the patients between two study groups during baseline to 55 minutes and at

Table 1 Baseline characteristics, duration, and blood loss in study patients ($n = 60$)

Variables	Concentration (mg/mL)						*p*-Value
	Group 1 (0.5 mg/mL [$n = 30$])			Group 2 (1 mg/mL ($n = 30$)]			
	Mean	SD	Median	Mean	SD	Median	
Age (years)	39.83	15.35	37.5	39.2	12.43	38	0.861
Weight (kg)	68.33	12.42	68	69.11	14.48	66.9	0.929
Height (cm)	161.24	8.19	162	161.03	8.45	163	0.767
BMI (kg/m^2)	26.26	4.31	25.59	26.68	5.31	26.86	0.626
Duration of anesthesia (minutes)	252.6	80.09	240	231.6	58.6	232.5	0.369
Duration of surgery (minutes)	178.17	62.58	170	168.03	53.14	157.5	0.806
Total blood loss (mL)	448.17	258.97	465	416.63	301.14	350	0.077

Abbreviations: BMI, body mass index; SD, standard deviation.
Independent samples *t*-test / Mann–Whitney U test used. $p < 0.05$ significant.

80 minutes and onward whereas difference was statistically significant at the time points of 60 minutes and 70 minutes ($p < 0.05$; ►**Fig. 3A** and **B**). Among other indices, SV and SVVs also did not vary among the groups throughout the study period. Hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure, MAPs, and ETCO2 readings) were similar among the two groups (►**Table 2**). However, the values of ETCO2 varied at 60 and 70 minutes ($p < 0.05$; ►**Table 2**; ►**Fig. 4**). The quality of the field of surgery and assessment of blood loss was performed using a standardized validated scale. Both the groups were comparable in terms of the quality of the surgical fields ($p = 0.549$). Usage of rescue drugs for treating hemodynamic perturbations was also compared and it was found to be similar in both the groups (►**Table 3**).

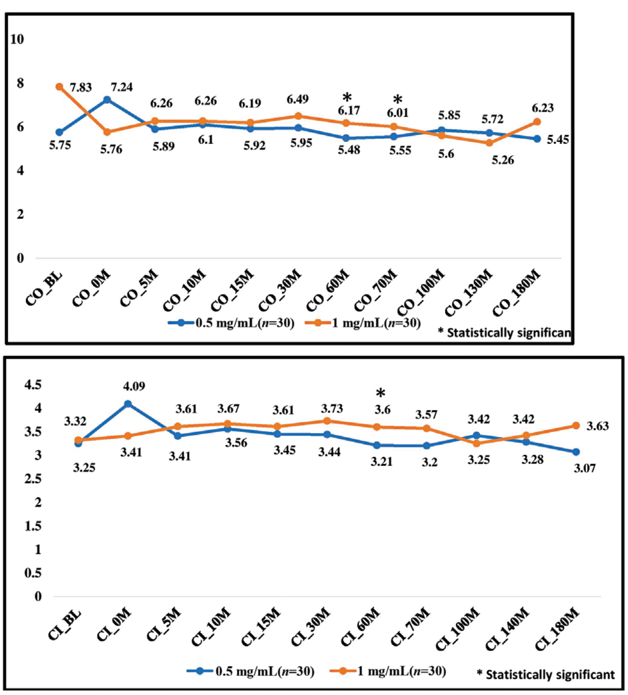

Fig. 3 (A) Distribution of cardiac output (CO) of the study groups. (B) Distribution of cardiac index (CI) of the study groups.

Discussion

Pituitary tumors are relatively common tumors with their frequencies depending on age (40–60 years) and sex (female preponderance).[9] Options for the treatment of pituitary adenomas include transsphenoidal surgical resection, irradiation, and medical therapy[10] Surgery is usually considered as the first-line treatment for large nonfunctioning adenomas with compression of the optic apparatus and majority of functioning tumors.[11] The transsphenoidal approach to the pituitary gland is frequently used because it is less invasive, provides direct access, and is faster.[12] Hemostasis is essential for the endoscopic visualization of anatomic structures and the avoidance of catastrophic injuries. Bleeding here is primarily capillary in origin and responds to local vasoconstrictors.[8]

In our study, adrenaline was topically administered in the nasal cavity for decongestion and invasive monitoring was performed to obtain accurate and precise hemodynamic data by measuring the maximum absolute change from baseline using a FloTrac device and Vigileo monitor. When CIs were compared in both the study groups, we found that baseline readings of the CO were higher in the group 2 patients (1:100,000) concentration in comparison to group 1 (1:200,000) patients. At the time of start of nasal packing with the cotton wicks soaked with different adrenaline concentrations, it was found that there was increase in mean values of CO in group 1 patients compared with group 2 but again 5 minutes after the endonasal packing, values of CO were found to be increased in group 2 (1:100,000) patients and remained consistently high throughout the dissection phase of the procedure. The values were found to be significant at 60 and 70 minutes of the surgery (►**Fig. 2A**). The CO trends dropped in group 2 patients (1:100,000) after the tumor was removed but again rose at the end of the surgery in comparison to group 1 patients

Table 2 Hemodynamic parameters during the perioperative course between the two groups

Sl.no.	SBP (mm Hg)			DBP (mm Hg)			MAP (mm Hg)			ETCO2 (mm Hg)		
	Group 1	Group 2	p	Group 1	Group 2	p	Group 1	Group 2	p	Group 1	Group 2	*p*-Value
BL	119.03 ± 19.68	116.83 ± 15.15	0.906	67.97 ± 11.71	67.77 ± 11.62	0.988	83.73 ± 12.33	84.53 ± 13.51	0.773	33.1 ± 3.2	32.95 ± 2.51	0.871
0	119.43 ± 19.48	122.67 ± 24.49	0.877	67.53 ± 11.18	71.87 ± 17.83	0.520	84.9 ± 13.33	88.6 ± 19.47	0.673	32.87 ± 2.5	32.23 ± 3.04	0.33
5	120.87 ± 18.74	123.73 ± 22.29	0.574	68.87 ± 12.70	73.47 ± 16.33	0.290	86.03 ± 13.61	90.07 ± 17.82	0.482	32.97 ± 2.43	32.7 ± 2.53	0.725
10	131.67 ± 64.16	120.2 ± 20.35	0.796	69.97 ± 13.26	69.77 ± 14	0.734	86.3 ± 16.35	85.5 ± 22.33	0.982	32.83 ± 2.39	32.6 ± 2.19	0.638
15	118.67 ± 25.83	114.8 ± 20.84	0.668	67.9 ± 15.73	66.03 ± 15.45	0.544	84.9 ± 19.75	83.03 ± 18.09	0.636	32.5 ± 2.13	32.33 ± 2.12	0.782
20	115.77 ± 17.44	115.83 ± 19	0.923	67.3 ± 12.86	68.03 ± 14.98	0.773	84.13 ± 13.14	83.4 ± 16.19	0.75	32.23 ± 2.11	32.4 ± 2.13	0.952
25	112.47 ± 15.51	112.43 ± 19.27	0.819	64.57 ± 11.21	65.17 ± 12.36	0.807	80.67 ± 12.27	80.27v14.55	0.668	32.37 ± 2.14	32.33 ± 2.14	0.905
30	109.23 ± 17.21	110.97 ± 15.16	0.446	61.47 ± 10.97	64.37 ± 10.46	0.248	77.17 ± 12.38	79.93 ± 11.55	0.219	32.03 ± 2.17	32.27 ± 2.38	0.599
35	110.5 ± 18.33	110.93 ± 17.82	0.75	63.33 ± 10.96	64.8 ± 12.48	0.871	79.4 ± 13.14	77.07 ± 18.26	0.584	32.07 ± 1.89	32.37 ± 2.2	0.627
40	106.93 ± 13.96	108.03 ± 15.43	0.615	60.97 ± 8.9	63.87 ± 11.34	0.287	76.2 ± 10.03	78.17 ± 12.83	0.7	32 ± 2.13	32.3 ± 2.35	0.457
45	107.5 ± 14.58	106.33 ± 14.54	0.871	61.4 ± 7.95	63.03 ± 10.18	0.750	77 ± 10.13	77.27 ± 11.53	0.882	31.9 ± 2.19	32.2 ± 2.46	0.417
50	109.73 ± 21.89	105.47 ± 13.18	0.888	62.63 ± 11.17	61.73 ± 9.85	0.796	78.4 ± 14.33	76.6 ± 10.29	0.888	32.1 ± 2.09	32 ± 2.6	0.94
55	107 ± 13.46	105.17 ± 13.7	0.574	61.9 ± 9.96	62.77 ± 12.11	0.982	77.27 ± 10.55	77.47 ± 13	0.813	32.07 ± 2.26	32.17 ± 2.82	0.794
60	104.77 ± 11.36	103.53 ± 13.68	0.491	60.6 ± 8.64	60.67 ± 9.25	0.976	75.67 ± 8.26	75.03 ± 10.6	0.62	32.53 ± 1.67	33.66 ± 1.39	0.006[a]
70	104. 9 ± 13.49	102.33 ± 13.57	0.433	60.6 ± 8.57	60.67 ± 9.8	0.929	72.49 ± 15.66	74.3 ± 10.27	0.801	32.84 ± 1.88	33.95 ± 1.04	0.011[a]
80	105.27 ± 25.53	100.55 ± 14.54	0.143	62.6 ± 11.07	57.93 ± 11.19	0.2	78 ± 12.93	72.34 ± 10.82	0.111	32.33 ± 2.45	32 ± 2.54	0.697
90	102.3 ± 14.09	102.62 ± 14.3	0.611	58.8 ± 8.47	60.93 ± 11.04	0.58	73.43 ± 9.57	73.45 ± 9.68	0.909	32.27 ± 2.59	32.24 ± 2.65	0.897
100	102.5 ± 13.07	100.25 ± 21.59	0.981	59.9 ± 11.76	60.71 ± 9.47	0.396	72.77 ± 10.36	74.79 ± 10.01	0.548	32.3 ± 2.72	32.21 ± 2.41	0.863
110	99.52 ± 10.69	103 ± 12.02	0.379	57.9 ± 9.05	61.11 ± 11.84	0.388	72.03 ± 9.23	74.64 ± 10.73	0.314	32.14 ± 2.55	32.14 ± 2.34	0.891
120	105.69 ± 12.6	102.89 ± 17.76	0.302	59.19 ± 10.47	59.59 ± 11.96	0.957	74.5 ± 10.66	74.48 ± 14.13	0.922	32.62 ± 2.84	32.41 ± 2	0.577
130	101.04 ± 21.31	101.88 ± 28.34	0.114	58.28 ± 4.87	59.46 ± 15.69	0.298	72.16 ± 5.9	73.75 ± 20.38	0.164	32.56 ± 2.57	32.37 ± 2.22	0.664
140	103.63 ± 14	102.65 ± 13.99	0.835	60.68 ± 8.2	60.35 ± 12.98	0.588	75.6 ± 8.36	73.35 ± 11.24	0.265	32.05 ± 2.59	32.57 ± 2.36	0.584
150	109.61 ± 16.81	101.41 ± 11.78	0.245	60.83 ± 8.65	62.24 ± 14.07	0.732	74.22 ± 7.56	72.88 ± 9.22	0.443	32.44 ± 2.91	31.88 ± 1.76	0.395
160	103.21 ± 17.52	103.33 ± 12.2	0.880	62.67 ± 12.36	61.87 ± 12.7	0.967	74.2 ± 15.34	72.8 ± 8.76	0.902	32.4 ± 3.04	32.4 ± 1.92	0.95
170	103.77 ± 12.77	113 ± 16.11	0.110	59.69 ± 7.85	67.5 ± 12.06	0.11	74.15 ± 8.31	79.17 ± 13.13	0.376	30.36 ± 8.64	33.17 ± 1.47	0.362
180	96.73 ± 15.55	112.2 ± 17.41	0.061	58.09 ± 9.89	64.6 ± 13.16	0.349	72 ± 11.16	80.6 ± 14.1	0.223	31.82 ± 3.28	32.5 ± 1.18	0.773
190	97.64 ± 9.17	108 ± 10.77	0.069	58.3 ± 6.46	61.86 ± 8.13	0.23	71.4 ± 6.11	79 ± 7.66	0.043	32.1 ± 3	33.29 ± 1.6	0.489

Abbreviations: BL, baseline; DBP, diastolic blood pressure; ETCO2, end-tidal carbon dioxide; MAP, mean arterial pressure; SBP, systolic blood pressure.
[a]Denotes statistical significance.

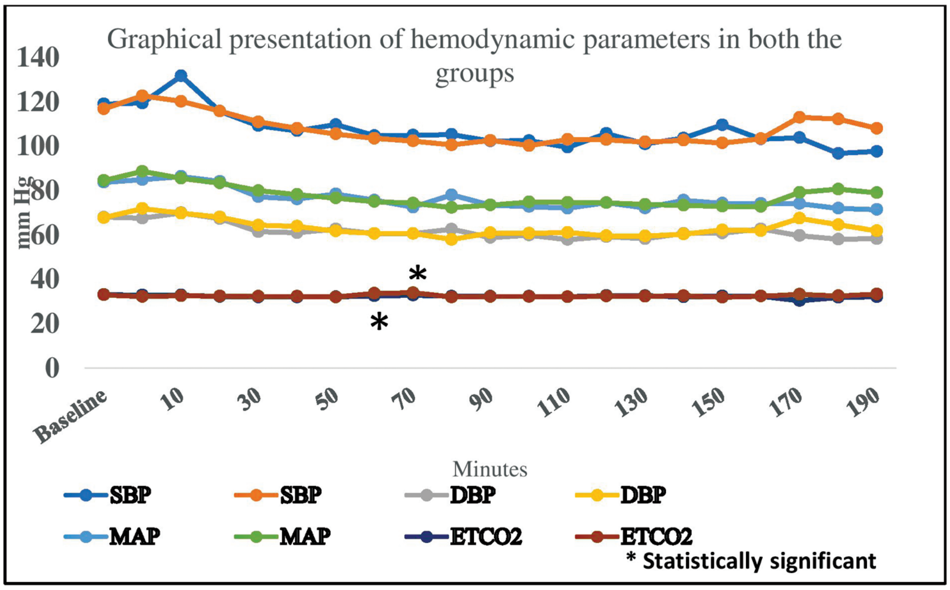

Fig. 4 Graphical presentation of hemodynamic parameters in both the groups. DBP, diastolic blood pressure; ETCO2, end-tidal carbon dioxide; MAP, mean arterial pressure; SBP, systolic blood pressure.

Table 3 Distribution of use of rescue drugs in the study group

Rescue drugs	Group 1 ($n = 30$)	Group 2 ($n = 30$)	p-Value
Metoprolol	10 (33.33%)	16 (53.33%)	0.121
Labetalol	15 (50%)	9 (30%)	0.117
Propofol	11 (36.67%)	10 (33.33%)	0.788
Mephentermine	8 (26.67%)	9 (30%)	0.777
Esmolol	1 (3.33%)	4 (13.33%)	0.165
None	7 (23.33%)	6 (20%)	0.756

Note: Chi-squared test/Fisher's exact test used. $p < 0.05$ significant.

(1:200,000). Similarly, Panda et al compared the COs using FloTrac monitor in functional endoscopic sinus surgery in 30 patients using two different concentrations of adrenaline (1 mg of adrenaline diluted in 20 mL normal saline in group 1 and 4 mg adrenaline diluted in 20 mL normal saline in group 2).[13] The numerical values of mean CO were found to be higher in group 2 patients compared with group 1 patients. They concluded that there was no significant difference in values of CO obtained (4.06 ± 0.161 vs. 4.145 ± 0.131).

CI was compared and no difference was observed in the patients between two study groups during baseline to 55 minutes and at 80 minutes and onward (each $p > 0.05$), whereas difference was statistically significant at the time points of 60 minutes and 70 minutes of the surgery in 1:100,000 concentration group (each $p < 0.05$) reflecting the similar trends of COs (►**Fig. 2B**).

In our study, we considered a systolic blood pressure greater than 20% of the baseline as a hypertensive response. Upon analyzing this parameter in isolation, we found a smaller proportion of patients in group 1 than in group 2 who exhibited an increase in systolic blood pressure of more than 20% from baseline (hypertensive response) following nasal mucosal instillation of adrenaline. This number could not reach statistical significance probably due to the small sample size. This suggests that the dose needed to reduce hypertensive responses could be considerably lower than either dose used by us in our study. Similar study conducted by Panda et al in 2012 observed consistently higher blood pressure in patients receiving high concentrations of adrenaline and also there was significant increase in the requirement of rescue drug used to treat hypertension in 4 mg adrenaline concentration group.[13] Bhatia et al found rise in blood group more than 20% of baseline in patients group receiving infiltration of 1:200,000 adrenaline with 2% lignocaine as compared with 1:400,000 concentration group.[14]

ETCO2 also showed a significant difference during the peak time of dissection phase at 60 and 70 minutes suggesting the proportional relationship between ETCO2 and CO (►**Fig. 4**). Additionally, adrenaline due to its effect on glycogen, fatty acid storage, activation of the adenylate cyclase (or cyclic adenosine monophosphate) cascade, results in glycogen and triacyl glyceride mobilization as well as a general increase in metabolic rate which causes an increase in carbon dioxide generation and consequently rise in ETCO2.[15] Likewise, Bhatia et al in their study had also reported a significant rise of ETCO2 from baseline values post-infiltration in both their groups.[14]

In our study, it was observed that the Boezaart grading of the quality of the surgical field and volume of blood loss estimated in the groups were similar (448.17 vs. 416.63 mL; ►**Table 1**). Panda et al observed 168 mL of blood loss in higher concentrations of adrenaline group in comparison to 426 mL in group receiving lower dose of adrenaline topically.[13] Lee et al in their study reported a mean blood loss of 333.9 mL in patients receiving 1:100,000 of epinephrine.[16] Cohen-Kerem et al assessed a mean blood loss of 203.5 mL when adrenaline (1:1000000) was infiltrated along with 1% lignocaine.[17]

Regarding the rescue drugs used to treat hemodynamic events that occurred during the procedure, they were found to be similar (►**Table 3**). In contrast, Panda et al[13] in their study had observed a significance increase in the requirement of rescue drugs to treat hypertension in patients receiving higher concentration of adrenaline. The mean infusion rate of nitroglycerine in group 2 (4 mg) was higher in comparison with that in group 1 (1 mg). There were few patients in the higher concentration of adrenaline who also required additional boluses of injection metoprolol.

Our study had certain limitations that deserved to be mentioned. First, we did not assess the catecholamine plasma concentrations, particularly of adrenaline and noradrenaline that would have provided us with a better estimate. Second, we had used a validated grading scale provided by Boezaart et al to assess intraoperative surgical field quality which the operating surgeon was comfortable with. This method has been criticized for compressing grading scores and failing to distinguish modest bleeding variances. The strengths of the study, on the other hand, were that it was an adequately powered study with sizeable number of participants. Second, a single surgeon performed all the surgeries to avoid any subjective bias. Third, invasive monitoring was used rather than noninvasive hemodynamic monitoring to provide precise information.

Conclusion

The use of topical adrenaline in ETSS appears to be a safe and successful way to achieve hemostasis, hence increasing the surgical visibility, and minimizing blood loss. The key to obtain cardio-stable hemodynamic parameters is to use a lowered concentration (1:200,000 solution) compared with the institutional standard concentration (1:100,000) that provides an optimal balance between the hemodynamic variables and a clear surgical field.

Conflict of Interest
None declared.

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