A Comparative Study of Nitroglycerine and Dexmedetomidine for Induced Hypotension in Functional Endoscopic Sinus Surgery

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ABSTRACT

BACKGROUND

We wanted to evaluate the efficacy of IV nitroglycerine and IV dexmedetomidine in achieving and maintaining induced hypotension in patients undergoing FESS under general anaesthesia, compare haemodynamic response in terms of heart rate, blood pressure, mean arterial pressure, compare clarity of the surgical field, compare the effect on duration of surgery and study the intraoperative and postoperative complications, if any.

METHODS

This is a randomised control trial conducted from 01/01/2018 to 31/12/2018 among 50 patients, ASA 1 & 2 undergoing FESS. They were randomly divided into 2 groups - group D (an infusion of dexmedetomidine was started with a loading dose of 1 µg / Kg over 10 min and thereafter was maintained between 0.5 - 1.0 µg / Kg / h) and group N (an infusion of nitroglycerine was started at the rate of 0.5 µg / Kg / min and was maintained between 0.5 - 2.0 µg / Kg / min). Haemodynamic data was recorded. Both the infusions were titrated to maintain a MAP between 65 and 75 mmHg. The visibility of the surgical site was checked by the surgeon at every 30 minutes using the Fromme and Boezaart scale.

RESULTS

Both groups consisted of 25 patients each and were demographically similar. In both groups heart rates remained within normal physiological limits, not requiring any pharmacological treatment. Both groups had comparable average MAP during surgery. The group D showed desirable attenuation of haemodynamic response at the time of intubation as well as at extubation. Both groups had comparable duration of surgery. Both the drugs were equally effective in creating clear surgical fields to the surgeons' satisfaction. Dexmedetomidine provided better intraoperative analgesia and reduced requirement of incremental fentanyl as compared to nitroglycerine. Emergence time was significantly higher in dexmedetomidine group.

CONCLUSIONS

Both the groups provided comparable clarity of surgical field with comparable haemodynamic parameters during surgery. dexmedetomidine provided better haemodynamic stability and an additional benefit of reduced requirement of intraoperative supplemental analgesia.

KEYWORDS

Induced hypotension, FESS, Dexmedetomidine, Nitroglycerine

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BACKGROUND

Rhinosinusitis, an important cause of significant discomfort and morbidity is commonly treated with FESS nowadays.[1,2,3] However, there can be serious complications associated with this procedure during peri-operative period like optic nerve injuries, infections, etc. whose incidence can increase with excessive bleeding during surgery.[4,5] Hence, it is mandatory to keep the surgical field clear of blood as far as possible to appreciate the different structures.

This can be achieved with the use of topical vasoconstrictors, local anaesthesia or induced hypotension with general anaesthesia.[6,7,8] Deliberate hypotension is defined as decreasing blood pressure 20 - 30 % below its baseline or reducing Mean Arterial Pressure (MAP) to 60 - 70 mmHg reversibly and maintaining the same throughout the surgery.

A variety of medications can be used to induce hypotension such as vasodilators like sodium nitroprusside,[9] nitroglycerine [10,11] and hydralazine; inhaled anaesthetics like isoflurane [12,13] and sevoflurane; beta adrenergic antagonists like esmolol.[9] Trimethaphan, adenosine and α2 agonists. nitroglycerine has been frequently used for induced hypotension during various surgeries, including nasal surgeries.[14,11] Dexmedetomidine has also gained wide acceptance for induced hypotension because of its sedation, analgesia and anxiolysis.[15,16,17] Therefore, this randomized study was planned using these two drugs intravenously for inducing and maintaining hypotension in patients undergoing FESS.

METHODS

This is a randomised control trial conducted from 01/01/2018 to 31/12/2018, carried out in 50 patients after taking informed written consent.

Inclusion Criteria

1. Patients scheduled for elective surgery.
2. Age between 18 to 55 years of both sexes.
3. Patients with ASA grade 1 or 2.

Exclusion Criteria

1. Patients with baseline heart rate < 60 bpm.
2. Patients with renal, hepatic or cerebral insufficiencies.
3. History of cardiac disease or hypertension.
4. Patients on treatment with beta blockers or calcium channel blockers.
5. PR interval > 0.24 seconds on ECG.
6. 2nd and 3rd degree heart block.
7. Patients with coagulopathies.
8. Patients on anti-coagulants.
9. History of drug addiction / chronic narcotic use.
10. Patients with allergy to study drugs.
11. Anticipated difficult airway.
12. Unanticipated difficult airway, requiring > 1 attempts at intubation or prolonged duration (> 15 sec) of laryngoscopy.
13. Patients who have undergone sinus surgeries before.
14. Patients having Hb < 10 mg / dl.
15. Patients with diabetes mellitus.
16. Patients with autonomic neuropathies.

Method of Study

- For all the patients Baseline data of heart rate, Blood pressure, mean arterial blood pressure, SPO2 were noted.
- All patients were premedicated with inj. Glycopyrrolate 0.004 mg / Kg IV, inj. Ondansetron 0.08 mg / Kg IV and inj. Fentanyl 1 µg / Kg IV before induction.

Patients were randomly allocated into 2 groups:-

Group D: An infusion of dexmedetomidine was made by adding 200 µg (2 mL) of dexmedetomidine to 48 mL of normal saline making a final concentration of 4 µg / mL. Infusion was started with a loading dose of 1 µg / Kg over 10 min.

Group N: An infusion of nitroglycerine was made by adding 25 mg (5 mL) of nitroglycerine to 45 mL of normal saline making a final concentration of 500 µg / mL. The infusion was started at the rate of 0.5 µg / Kg / min.

- The respective infusion was started as loading dose 10 minutes before induction of anaesthesia and was completed before the induction. The maintenance dose was continued, and haemodynamic data was recorded.
- All patients were preoxygenated with 100 % oxygen.
- Patients were induced with inj. Thiopentone Sodium 2.5 % IV 5 mg / Kg.
- After confirming the ability to ventilate, inj. Suxamethonium 2 mg / Kg IV was given to facilitate laryngoscopy and intubation.
- Patients were intubated with appropriate sized cuffed endotracheal tube and an oropharyngeal pack was kept after the intubation.
- Intubations were done within 15 seconds of laryngoscopy in single attempt.
- Both the infusions were titrated to maintain a MAP between 65 and 75 mmHg and then infusion rate was kept constant throughout the surgery.
- Rate of dexmedetomidine infusion was kept 1 µg / Kg for 10 minutes as loading dose and thereafter 0.5 µg / Kg / h. (0.5 - 1.0 µg / Kg / h)
- Rate of NTG infusion was kept 0.5 µg / Kg / min. (0.5 - 2.0 µg / Kg / min)
- Anaesthesia was maintained with O_2 (50 %), N_2O (50 %), Sevoflurane 1.5 % and inj. Vecuronium 0.08 mg / Kg loading dose and 0.02 mg / Kg top up doses.
- An additional dose of fentanyl 1 µg / Kg was given intra-operatively when there was an increase in HR > 20 % and MAP > 20 % from baseline values.
- Vitals monitored were heart rate, blood pressure, mean arterial pressure and SPO_2.
- All parameters were recorded at regular intervals i.e. at baseline, before induction, after intubation, after 5 min,

10 min, 15 min, 30 min of intubation and thereafter every 15 mins till the end of surgery, at the time of reversal and at extubation.
- To further reduce the amount of surgical bleeding and for surgeon's convenience, all the patients were positioned in approx. 30° reverse Trendelenburg position. Local infiltration of lignocaine (2 %) + adrenaline (1:100,000) mixture was done in in all patients.
- Visibility of the operative field was assessed by the operating surgeon every 30 minutes intraoperatively and at the end of the surgery according to the Fromme and Boezaart scale. The score was explained to the surgeon.
- Intraoperatively, HR < 60 BPM was treated with 0.5 mg atropine IV.
- 50 % reduction in the infusion dose was done where MAP was less than 65 mmHg. IN case of no response the infusion was stopped completely. Mephentermine 6 mg IV was given to treat resistant hypotension.
- Five minutes before the completion of surgery, all the study drugs were discontinued.
- At the end of surgery, neuromuscular blockade was reversed with inj. Glycopyrrolate (0.008 mg / Kg) and inj. Neostigmine (0.05 mg / Kg) IV and oral pack was removed.
- Extubation was carried out when the patients had adequately recovered from the effect of neuromuscular blockade with regular breathing pattern, good muscle power / tone and were able to respond to verbal commands.
- Heart rate, blood pressure, mean arterial pressure, SPO2 and respiratory rate were recorded at 5 min, 30 min, 60 min, 90 min, and 120 min after extubation. Postoperative sedation was also assessed with Ramsay Sedation Score at those times.
    1. Anxious, agitated, restless.
    2. Cooperative, oriented, tranquil.
    3. Responsive to commands only.
    4. Brisk response to light glabellar tap or loud auditory stimulus.
    5. Sluggish response to light glabellar tap or loud auditory stimulus.
    6. No response to light glabellar tap or loud auditory stimulus
- Any other complaints like nausea, vomiting, headache, restlessness, pruritus, bradycardia (heart rate < 60 BPM), hypotension (MAP < 65 mmHg) and allergic reaction were noted.
- Incremental fentanyl consumption and duration of surgery were recorded. Emergence time was also recorded.
- The results were expressed as mean ± SD. Statistical analysis was done using unpaired t test and p value less than 0.05 was considered as significant and less than 0.001 was considered as highly significant and more than 0.05 was considered as not significant.

RESULTS

This study was conducted to compare effect of IV dexmedetomidine and IV nitroglycerine for induced hypotension during FESS. In the present study all patients were between 18 yrs. to 55 yrs. of age, belonging to ASA grade 1 or 2. Both groups were demographically similar.

Time	Group D	Group N	P Value	Inference
Baseline	76.52 ± 4.70	74.56 ± 4.96	> 0.05	NS
Before Induction	68.96 ± 4.8	86.32 ± 4.01	< 0.05	S
After Intubation	73.64 ± 3.97	89.96 ± 3.81	< 0.05	S
Intubation+ 5 min	69.12 ± 3.40	81.96 ± 3.81	< 0.05	S
Average during Surgery	70.89 ± 4.05	77.82 ± 8.49	< 0.05	S
At Extubation	76.96 ± 3.22	85.88 ± 3.89	< 0.05	S
Extubation+ 5 min	72.8 ± 2.73	78.56 ± 4.96	< 0.05	S

Table 1. Mean Heart Rate (/min) at Different Time Intervals

According to Table 1 there was no significant variation in baseline heart rates in both the groups.

Any fluctuations in heart rate after starting of study drug were below the baseline values in group D and were above the baseline values in group N.

Table 4 shows that both groups had similar baseline MAP values. Infusion rate was kept constant once the target MAP (65 - 75 mmHg) was achieved during surgery.

Average MAP during the surgery was comparable for both the groups (NS). There were larger fluctuations in Group N as compared to Group D at all the stages except during surgery.

	Group D	Group N	P Value	Inference
Mean Duration	74.68	80	> 0.05	NS
SD	12.45	10.16		

Table 2. Duration of Surgery (in Minutes)

Time Interval	Group D	SD Group D	Group N	SD Group N	P Value	Inference
I + 30	2.24	0.43	2.2	0.40	> 0.05	NS
I + 60	2.44	0.71	2.48	0.58	> 0.05	NS
I + 90	3	0.70	3.16	0.75	> 0.05	NS
Overall	2.37	0.47	2.32	0.47	> 0.05	NS

Table 3. Clarity of Surgical Field-Fromme Boezaart Score (0 - 5)

Time	Systolic Blood Pressure		Diastolic Blood Pressure		Mean Arterial Pressure			
	Group D	Group N	Group D	Group N	Group D	Group N	P Value	Inference
Baseline	123.76 ± 6.09	121.36 ± 5.31	81.12 ± 6.69	81.44 ± 6.33	95.33 ± 6.20	94.74 ± 5.63	> 0.05	NS
Before Induction	108.32 ± 5.31	101.36 ± 5.31	69.12 ± 6.69	61.2 ± 5.06	82.19 ± 5.82	74.58 ± 4.69	< 0.001	HS
After Intubation	112.4 ± 4.62	117.36 ± 5.31	73.92 ± 3.85	72.2 ± 5.06	86.75 ± 3.52	90.58 ± 4.69	< 0.001	HS
Intubation + 5 min	103.76 ± 4.63	99.6 ± 4.08	64.72 ± 2.94	59.76 ± 4.37	77.73 ± 2.96	73.04 ± 3.70	< 0.001	HS
Avg during Surgery	100.82 ± 7.42	100.00 ± 8.79	58.36 ± 9.70	59.05 ± 8.11	72.52 ± 8.27	72.70 ± 7.86	> 0.05	NS
At Extubation	118.56 ± 3.81	121.76 ± 3.66	78.96 ± 5.23	81.32 ± 5.29	92.16 ± 3.90	94.80 ± 4.47	< 0.05	S
Extubation + 5 min	115.6 ± 4.16	116.96 ± 2.58	74.32 ± 2.69	77.32 ± 5.29	88.08 ± 2.69	90.53 ± 4.08	< 0.05	S

Table 4. Blood Pressure (mmHg) at Different Time Intervals (Intraoperatively)

Incremental Fentanyl Requirement	Group D (n = 25)	Group N (n = 25)
No. of Patients	0	8

Table 5. Requirement of Incremental Doses of Fentanyl

Emergence time was significantly higher for the dexmedetomidine group. Post-operative vitals are similar in both the groups. Also, there is no postoperative respiratory depression in either of the groups. No complications occurred intraoperatively or postoperatively in either of the groups.

DISCUSSION

Now a days, rhinosinusitis is commonly treated with FESS.[1,2,3] Intraoperatively, spikes in MAP may lead to increased capillary oozing. On the contrary, very low pressures may lead to complications like prolonged awakening, cerebral thrombosis, brain infarctions, acute renal failure. Hence, haemodynamic stability during surgery is mandatory. Maintenance of adequate depth of anaesthesia is also important to avoid surges in blood pressure and thus reduce blood loss and produce a clearer operative field. Various techniques have been described for this.

One of such techniques is controlled reduction in blood pressure.[18] to such levels so that bleeding is minimal, without compromising perfusion of vital organs. This is the basic concept for induced hypotensive anesthesia.[19] Reduced bleeding improves the visibility of the surgical field, decreases manipulations, lessens complications and shortens the operative time.[20,9]

dexmedetomidine, a selective α2 adrenoceptor agonist, causes reduction in BP and HR, sedation and analgesia. Hall JE et al[21] studied the sedative, amnestic, and analgesic properties of small dose dexmedetomidine infusions and showed that it has minimal respiratory depressant effect with potent sedative and analgesic effects compared to opioids and other sedatives.

Various studies have shown that dexmedetomidine decreases bleeding in surgeries within the framework of haemodynamic stability.[22,23,24,16,17] Guven et al.[25] reported better haemodynamic stability and improved surgical field when dexmedetomidine was used in FESS for conscious sedation.

Cincikas and Ivaskevicius [26] used nitroglycerine infusion to maintain MAP of 50 - 60 mmHg during endoscopic nasal surgery and observed reduced bleeding and improved surgical field quality.

In our study we compared IV dexmedetomidine and IV nitroglycerine for induced hypotension in FESS. Our target was to reduce MAP to 65 - 75 mm Hg, which is considered as moderate controlled hypotension.[26,27]

Both the study groups were comparable in age, ASA grade, male : female ratio and weight. Both groups consisted of 25 patients each, selected at random.

The baseline heart rate values of both the groups were comparable. Starting from before induction till 5 minutes after extubation, heart rate was higher in group N. (HR group N > group D), which was statistically significant ($p < 0.05$). Yet, in both groups the heart rates remained within physiological limits.

This might be due to reflex tachycardia associated with nitroglycerine infusion. Lower heart rates with dexmedetomidine might be due to its sympatholytic effect.

Similar results were found by SJS Bajwa et al[28] who studied nitroglycerine, Esmolol and dexmedetomidine for induced hypotension during FESS.

In our study the target MAP was maintained between 65 - 75 mmHg during the surgery. Kol et al.[23] studied Controlled hypotension during tympanoplasty in adults and found that liver and kidney functions were not affected where the target MAP was 65 - 75 mmHg.

In our study there were more fluctuations in MAP in group N than group D. It suggests that dexmedetomidine is effective in blunting the haemodynamic response of laryngoscopy and extubation. dexmedetomidine provides better haemodynamic stability as compared to nitroglycerine.[18,29]

There is a close relationship between reduced MAP and surgical field clarity in surgical procedures as observed by Sieskiewicz A.[30]

In present study, equal efficacy of both drugs in decreasing the intraoperative MAP provided comparable surgical fields as suggested by the similar Fromme and Boezaart scores and durations of surgery.

Duration of surgery in Group D was 74.68 ± 12.45 minutes and in Group N was 80 ± 10.16 minutes. The difference was statistically non-significant.

Similar findings were achieved by SJS Bajwa et al.[28]

In our study the clarity of the operative field was assessed by the surgeon according to the Fromme and Boezaart scale.[8] There was no significant difference between the 2 groups at any point of time. From me and Boezaart score 2 - 3 is usually considered ideal.[31,16]

In present study, the amount of actual blood loss was not measured because usually in FESS small quantity of blood is lost. Our focus was on the clarity of surgical field.

50 µg Fentanyl was given when there was > 20 % increase in heart rate and > 20 % increase in MAP. None of the patients from Group D required incremental fentanyl intraoperatively, whereas 6 out of 25 patients from group N required incremental dose of fentanyl. This might be due to the analgesic efficacy of dexmedetomidine.[32]

Huncke TK et al[33] conducted a study evaluating the efficacy of dexmedetomidine for sedation and found that total dose of fentanyl was significantly less during the DEX infusions.

Emergence time, defined as the interval between stop page of the anaesthetic agents to eye opening on verbal command was also recorded. Similar to S.J.S. Bajwa et al[28] emergence time in Group D (7.32 ± 1.1 min) was statistically significantly higher as compared to Group N (4.12 ± 1.16 min). This might be due to its sedative property of dexmedetomidine which is mediated through its action in the locus ceruleus.[34]

Post-operative vitals in both the groups, i.e. heart rate, MAP, SPO_2 and respiratory rates did not show any statistically significant difference. As the respiratory rates were similar in both the groups post-operatively, we can accept that dexmedetomidine does not cause significant post-operative respiratory depression.

Post-operative sedation scores were recorded at 5, 30, 90 and 120 minutes after extubation. dexmedetomidine does not cause statistically significant sedation in post-operative period.

Side effects such as bradycardia, hypotension, allergic reactions were considered intraoperatively and nausea / vomiting, hypotension / hypertension, bradycardia / tachycardia, shivering, dry mouth, gastrointestinal system disorders, blurry vision, allergy, pruritus, headache were considered during the post-operative period.

There were no complications / side effects observed in either of the study groups at any time.

CONCLUSIONS

Both groups provided comparable clarity of surgical field with comparable haemodynamic parameters intraoperatively. Dexmedetomidine provided better haemodynamic stability than nitroglycerine and an additional benefit of reduced requirement of intraoperative supplemental analgesia. But emergence time was higher in dexmedetomidine group compared to nitroglycerine group.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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