Nitroglycerine, esmolol and dexmedetomidine for induced hypotension during functional endoscopic sinus surgery: A comparative evaluation

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Abstract

**Background and Aim:** Induced hypotension limits intra-operative blood loss to provide better visibility of the surgical field and diminishes the incidence of major complications during functional endoscopic sinus surgery (FESS). We aimed at comparing nitroglycerine, esmolol and dexmedetomidine for inducing controlled hypotension in patients undergoing FESS.

**Material and Methods:** One hundred and fifty American Society of Anesthesiologists physical status I or II adult patients undergoing FESS under general anesthesia were randomly allocated to three groups of 50 patients each. Group E received esmolol in a loading and maintenance dose of 1 mg/kg over 1 min and 0.5-1.0 mg/kg/h, respectively. Group D received a loading dose of dexmedetomidine 1 μg/kg over 10 min followed by an infusion 0.5-1.0 μg/kg/h, and group N received nitroglycerine infusion at a dose of 0.5-2 μg/kg/min so as to maintain mean arterial pressure (MAP) between 60 and 70 mmHg in all the groups. The visibility of the surgical field was assessed by surgeon using Fromme and Boezaart scoring system. Hemodynamic variables, total intra-operative fentanyl consumption, emergence time and time to first analgesic request were recorded. Any side-effects were noted. The postoperative sedation was assessed using Ramsay Sedation Score.

**Result:** The desired MAP (60-70 mmHg) could be achieved in all the three study groups albeit with titration of study drugs during intra-operative period. No significant intergroup difference was observed in Fromme’s score during the intra-operative period. The mean total dose of fentanyl (μg/kg) used was found to be significantly lower in group D compared to groups E and N (1.2 ± 0.75 vs. 3.6 ± 1.3 and 2.9 ± 1.1 respectively). The mean heart rate was significantly lower in group D compared to groups E and N at all times of measurement (P < 0.05). The MAP was found to be significantly lower in group D compared to groups E and N after infusion of study drugs, after induction, just after intubation and 5 min after intubation (P < 0.05). The Ramsay Sedation Scores were significantly higher in group D (score 3 in 46%) when compared to group E (score 2 in 50%) and group N (score 2 in 54%) (P < 0.001). The emergence time was significantly lower in group E and group N compared to group D. Time to first analgesic request was significantly longer in group D.

**Conclusion:** Dexmedetomidine and esmolol provided better hemodynamic stability and operative field visibility compared to nitroglycerin during FESS. Dexmedetomidine provides an additional benefit of reducing the analgesic requirements and providing postoperative sedation.

**Key words:** Controlled hypotension, dexmedetomidine, esmolol, functional endoscopic sinus surgery, nitroglycerine

Introduction

Rhino-sinusitis, an important cause of significant discomfort and morbidity is commonly treated with FESS nowadays. However, there can be serious complications associated with this procedure during peri-operative period like orbital cellulitis, optic nerve injuries, meningitis, etc. whose incidence can increase with excessive bleeding during surgery. Hence, it is mandatory to keep the surgical field as free of blood as possible to improve visibility of anatomical landmarks and structures. This can be achieved with the use of topical vasoconstrictors, with local anesthesia or use of controlled hypotension with general anesthesia.
Controlled hypotension involves reducing arterial blood pressure 30-40% below its normal range or reducing mean arterial pressure (MAP) to 65 mmHg reversibly and maintaining it at that level throughout the surgery. A variety of medications can be used to induce intraoperative hypotension including vasodilators like sodium nitroprusside, nitroglycerin and hydralazine; inhaled anesthetics like isoflurane and sevoflurane; intravenous anesthetics like propofol; beta adrenergic antagonists like esmolol; trimethaphan, adenosine and α2 agonists. Some of the reported disadvantages with the use of these agents include resistance to vasodilators, tachyphylaxis with nitroglycerin, cyanide toxicity with the use of nitroprusside and delayed recovery from anesthesia with the use of high doses of inhaled anesthetics.

Esmolol and nitroglycerine have been frequently compared for controlled hypotension during nasal surgery. Dexametomidine has also gained wide acceptance for induced hypotension because of its sedation, analgesia and anxiolysis. There are no studies comparing the efficacy of these three drugs in achieving controlled hypotension. Therefore, this randomized study was planned using these three drugs for inducing and maintaining controlled hypotension in patients undergoing functional endoscopic sinus surgery (FESS) under general anesthesia.

**Material and Methods**

This prospective randomized study was carried out after the approval of Institutional Ethics Committee. Hundred and fifty patients belonging to American Society of Anesthesiologists physical status class I or II, aged between 18 and 55 years and posted for elective FESS under general anesthesia were included in the study. Fifty patients were allocated to each of the three groups randomly, based on computer generated numbers. The operating surgeon and the anesthesiologist doing the peri-operative monitoring were blinded to the study drug by wrapping the syringes with number codes. Patients with uncontrolled hypertension, cardiovascular diseases including rhythm disturbances, renal or hepatic dysfunction, coagulation defects or patients on medications affecting coagulation system were excluded from the study.

A thorough preanesthetic evaluation was performed and an informed written consent was taken from all the patients by the investigator a day prior to the surgery. The patients received nil per oral instructions as per the standard protocol and were premedicated with alprazolam 0.25 mg and ranitidine 150 mg orally in the night and in the morning of day of surgery. After shifting the patients to the operating room, noninvasive blood pressure, five lead electrocardiography and pulse oximetry were started. Baseline vitals were recorded including heart rate (HR), MAP and oxygen saturation. After securing an intravenous line, preloading was carried out with lactated ringer’s solution 5 ml/kg. The patients were randomly allocated by computer generated numbers in to three groups:

- **Group D**: Received dexametomidine loading dose of 1 μg/kg given over 10 min, followed by a continuous infusion of 0.5-1.0 μg/kg/h.
- **Group N**: Received an infusion of nitroglycerine 0.5-2 μg/kg/min.
- **Group E**: Received a loading dose of esmolol 1 mg/kg infused over 1 min, followed by a continuous infusion of 0.5-1.0 mg/kg/h.

All the infusions were titrated to maintain a MAP between 60 and 70 mmHg.

The loading doses of dexametomidine and esmolol were administered before the induction of anesthesia. Nitroglycerine was started as infusion without any bolus dose. The duration of infusion was constant in all the three groups. The induction of anesthesia was done with thiopentone sodium 5 mg/kg and fentanyl 2 μg/kg, followed by vecuronium 0.1 mg/kg intravenously. After tracheal intubation, anesthesia was maintained with one minimum alveolar concentration isoflurane in nitrous oxide and oxygen mixture (60:40) and top-up doses of vecuronium as and when required. An oropharyngeal pack was kept after the intubation. An additional dose of fentanyl 1 μg/kg was given intra-operatively with an increase in HR and MAP of more than 20% from baseline values.

To further reduce the amount of surgical bleeding and for surgeon’s convenience, all the patients were positioned in approx. 30° reverse trendelenburg position. Two ml of lignocaine-adrenaline (1:100,000) mixture was infiltrated at the surgical site by the surgeon in all the patients.

Heart rate, MAP, SpO2 and EtCO2 were monitored throughout the surgery and recorded at baseline, after loading dose of the study drug, after induction, after intubation, 5 min after intubation, at an interval of 5 min intra-operatively, after reversal, after extubation and 5 min after extubation. HR <45 beats/min was considered as bradycardia, and was managed with 0.5 mg atropine intravenously. MAP <60 mmHg was initially managed with a 50% reduction in the infusion dose of the study drug and further stoppage of the infusion if no response was obtained in 5 min. Mephentermine 6 mg intravenously was administered for the resistant hypotension.
The visibility of the operative field was assessed by the surgeon according to the scale proposed by Fromme and Boezaart.\[16\]

Five minutes before the end of surgery, all the study drugs were discontinued. At the end of the surgery, the nasal packing was done keeping a cut piece of small size endotracheal tube to allow the patient to breathe through the nose postoperatively.\[17\] The residual neuromuscular blockade was antagonized with neostigmine 0.05 mg/kg and glycopyrrolate 0.1 mg/kg intravenously and extubation was done when the patient was fully awake, breathing regularly with adequate tidal volume. Total intra-operative fentanyl consumption, duration of surgery and total anesthesia time were recorded. Emergence time, defined as the interval between discontinuation of the anesthetics to response of eye opening to the verbal command,\[18\] was also recorded. The postoperative sedation was assessed with Ramsay Sedation Score.\[19\] The postoperative side-effects such as nausea and vomiting, shivering and dry mouth were observed and recorded. The time for the first analgesic request after the surgery was also recorded.

**Table 1: The demographic variables**

| Demographic variable             | Group D (n = 50) mean ± SD | Group N (n = 50) mean ± SD | Group E (n = 50) mean ± SD | P   |
|---------------------------------|----------------------------|----------------------------|----------------------------|-----|
| Age (years)                     | 31.6±5.2                   | 36.4±6.1                   | 34.3±5.6                   | —   |
| Gender (male/female)            | 31/19                      | 35/15                      | 38/12                      | —   |
| ASA-physical status (I/II)      | 39/11                      | 36/14                      | 33/17                      | —   |
| BMI                             | 28.4±1.7                   | 27.1±1.4                   | 26.9±2.1                   | —   |
| Duration of surgery (min)       | 133±32                     | 141±37                     | 148±29                     | 0.92|
| Total anesthesia time (min)     | 146±32                     | 152±29                     | 138±38                     | 0.88|
| Mean dose of fentanyl (μg/kg)   | 1.2±0.75                   | 3.6±1.3                    | 2.9±1.1                    | <0.001|
| Emergence time (min)            | 7.6±1.4                    | 4.4±1.2                    | 4.5±1.3                    | <0.001|
| Time to first analgesic request (min) | 60.5±9.2       | 31.7±5.5                   | 30.4±5.3                   | <0.001|

*BMI = Body mass index, SD = Standard deviation, ASA = American Society of Anesthesiologists*

**Table 2: Comparison of mean HR (per minute) in group D, N and E**

| Time of measurement (beats/min) | Group D (n = 50) | Group N (n = 50) | Group E (n = 50) | P   |
|---------------------------------|-----------------|-----------------|-----------------|-----|
| Baseline                        | 75.6±8.3        | 74.2±9.2        | 76.4±7.5        | 0.78|
| After loading dose of study drug| 66.7±3.8        | 84.2±5.6        | 71.3±5.3        | <0.001|
| After induction of anesthesia   | 67.3±4.9        | 88.2±5.6        | 72.1±4.8        | <0.001|
| After intubation                | 72.6±5.4        | 89.4±6.3        | 75.8±4.5        | <0.001|
| 5 min after intubation          | 68.4±4.4        | 82.6±6.5        | 71.8±4.9        | <0.001|
| Average intraoperatively        | 70.4±5.2        | 78.2±5.4        | 72.8±3.9        | 0.031|
| After reversal                  | 72.6±6.6        | 84.4±7.2        | 77.4±4.6        | 0.022|
| After extubation                | 76.4±6.2        | 85.8±9.4        | 78.4±6.2        | 0.009|
| 5 min after extubation          | 71.7±5.2        | 78.6±6.7        | 73.6±5.8        | 0.023|

*HR = Heart rate*

**Results**

A total of 150 patients were included in the study and were divided randomly into three groups of 50 patients each (n = 50).

The demographic variables among the three groups are shown in Table 1 and there was no statistically significant difference among the three groups with regard to demographic variables, duration of surgery and total anesthesia time. The mean total dose of fentanyl in μg/kg used was significantly lower in group D compared to groups N and E (1.2 ± 0.75 vs. 3.6 ± 1.3 and 2.9 ± 1.1 respectively) [Table 1].

The mean HR was significantly lower in group D compared to groups N and E at all the times of measurements (P < 0.05) [Table 2].

The MAP was significantly lower in group D compared to groups N and E after infusion of study drugs, after induction
of anesthesia, after intubation and 5 min after intubation \((P < 0.05)\) [Table 3]. However, the desired MAP for intra-operative induced hypotension could be achieved in all the three groups. There was no statistically significant difference in the Fronne’s score in the three groups. None of the patients experienced bradycardia, resistant hypotension or hypertension during the study period. None of them required additional atropine or mephentermine.

The emergence time was significantly shorter in group E and group N compared to group D [Table 1].

No serious side-effects were observed in any of the three groups. The incidence of nausea and vomiting was comparable in the three groups. The major side-effect observed in group D was dry mouth (26%) [Table 4]. The Ramsay Sedation Scores were significantly higher in group D compared with groups N and E with majority of patients having a sedation score of 3 (46%) in group D while most of the patients had a score of 2 in groups N and E (54% in group N and 50% in group E) [Table 5] two patients in group D had sedation score of 5 and were deeply sedated. The time to first analgesic request was significantly prolonged in group D when compared to other groups [Table 1].

**Discussion**

An important technique to reduce bleeding during the surgery is controlled reduction in blood pressure to such levels so that bleeding is minimal, but at the same time perfusion to the vital organs is well-maintained. This is the underlying concept for controlled hypotensive anesthesia.\(^{[20]}\) Reduced bleeding in the operative site improves the quality of the surgical field, decreases the number of manipulations as well as the incidence of major complications and shortens the surgical time.\(^{[10,21]}\)

Dexmedetomidine, a selective \(\alpha_2\) adrenoceptor agonist, causes reduction in blood pressure, slowing of HR, sedation and analgesia. The fall in blood pressure is mainly due to inhibition of central sympathetic outflow and also due to stimulation of presynaptic \(\alpha_2\) adrenoceptors decreasing norepinephrine release.\(^{[22]}\) An important advantage is its minimal respiratory depressant effect with potent sedative and analgesic effects compared with opioids and other sedatives. A few studies have shown that dexmedetomidine decreases the bleeding in surgeries within the framework of hemodynamic stability.\(^{[11,13,14,23]}\)

The heart rate was higher in group N due to reflex tachycardia associated with nitroglycerine infusion. Dexmedetomidine caused a lower heart rate due to its sympatholytic effect.\(^{[24]}\)

The MAP also showed a significant reduction in group D compared to group N and E, but only at three observation times, that is, after induction of anesthesia, after intubation and 5 min after intubation. This observation suggested that dexmedetomidine is effective in blunting the hemodynamic response of stress during laryngoscopy as has been shown by other studies.\(^{[25,26]}\) The MAP however, was equally lowered in all the three groups suggesting equal efficacy of all the three drugs in lowering the MAP, thereby providing comparable surgical field as suggested by the Fromme and Boezaart’s score.

Cincikas and Ivaskevicius\(^{[27]}\) used nitroglycerine infusion...
(0.79 ± 0.34 μg/kg/min) to maintain MAP of 50-60 mmHg during endoscopic nasal surgery and observed reduced surgical bleeding and improved surgical view quality. Guven et al.[28] used dexmedetomidine for conscious sedation for FESS and reported better hemodynamic stability and improved surgical field.

The analgesic efficacy of dexmedetomidine has been appreciated in diverse settings.[29-33] Similarly, we found that intra-operative fentanyl requirement was significantly reduced in the dexmedetomidine group as compared to the other two groups. The patients in group D had a longer emergence time, as reported in other studies as well.[11,34]

We also observed a significant delay in the first postoperative analgesic request in group D as compared to the other two groups. It has been shown that perioperative analgesic requirements are significantly reduced with intra-operative use of dexmedetomidine infusion.[11,35] The patients in the dexmedetomidine group had significantly higher sedation scores compared to group N and E. Shams et al.[11] also reported higher postoperative sedation scores with the intraoperative use of dexmedetomidine. The sedative and analgesic sparing effects of dexmedetomidine are mediated through its action in the locus coeruleus and dorsal horn of spinal cord respectively.[36] The postoperative sedation is often desirable, but may sometimes prolong the emergence time.[34] The incidence of postoperative shivering was significantly lower in the dexmedetomidine group, as acknowledged earlier also.[37] The most frequent reported side-effect with dexmedetomidine is dry mouth, which is not bothersome and can be easily managed.

**Conclusion**

Dexmedetomidine and esmolol provided better hemodynamic stability and comparable operative field visibility to nitroglycerine during FESS. Dexmedetomidine provides an additional benefit of reducing the analgesic requirements and providing postoperative sedation.

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**Conference Calendar April 2016**

| Name of conference | Dates        | Venue                          | Name of organising Secretary with contact details |
|--------------------|--------------|--------------------------------|---------------------------------------------------|
| 6th Annual Conference of the Academy of Regional Anaesthesia (AORA) AORA INDIA 2016 | September 23rd-24th, 2016 | Hyderabad | Dr. TVS Gopal Organising Chairperson |
| NYSSORA 15th Annual Symposium on Regional Anesthesia, Pain and Perioperative Medicine 2016 (NYSSORA 2016) | September 23rd-25th, 2016 | Hilton Midtown, New York | health@nyssora.com www.nyssora.com |
| ISACON Bihar Jarkhand – 2016 Annual State Conference of ISA Bihar Jarkhand State Chapter, | September 23rd-25th, 2016 | The Park, Juba Sahni Park Market, Club Road, Mithanpura, Muzaffarpur | Org Secretary: Dr. Narendra Kumar Mobile No.: +91-9431650905 / 7250514526 Email: narendrak792@gmail.com |
| ISACON GUJARAT – 2016 & WIZACON 2016 49th Annual State Conference of ISA GUJARAT State Chapter & 12th West Zone Conference | September 23rd-25th, 2016 | Rangoli Hotel & Resorts, Vertej, Bhavnagar | Org Secretary: Dr. Fremiot J. Mascarenhas Mobile No.: +91-9428401780 Email: drfremiot@hotmail.com/isacongujarat2016@gmail.com Website: www.isacongujarat2016.com |
| 40th Annual State Conference of ISA Kerala State Chapter 2016 ISACON Kerala 2016 | October 7th-9th, 2016 | MAC FAST Auditorium, Tiruvalla, Pathanamthitta, India | Dr. Koshy Thomas Phone: 91-9447398170 E-mail: thomaskoshy59@gmail.com |
| 9th National Conference of Association of Obstetric Anaesthesiologists AOA-MASCON 2016 | October 14th-16th, 2016 | The Renaissance, Powai, Mumbai, India | Dr. Satish Kulkarni, Dr. Manju Sinha, Dr. Vijay Shetty Organising Secretaries Dr. Mayuri Shetty The Secretariat, AOA-MASCON 2016 Vikas Paradise, Tower I, A-1402, L.B.S. Road, Mulund (W). Mumbai - 400 080. Maharashtra, INDIA. Mobile: 09820185527, E-mail: aoamumbai2016@gmail.com Website: www.mumbaiana.org / www.aoaindia.com |