Dexmedetomidine versus Nitroglycerin for Controlled Hypotensive Anaesthesia in Functional Endoscopic Sinus Surgery

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Abstract

Context: In patients with chronic sinusitis, Functional Endoscopic Sinus Surgery (FESS) is the preferred surgical option as part of treatment after conservative measures have failed.

Aims: To improve the success of this surgery and to minimize complications, bloodless field is required. So our primary objective will be to provide bloodless field intraoperatively.

Settings and design: Our study was a single blinded, prospective, randomized and comparative clinical study. It included forty adult patients between 18-60 years of age and of either sex. They all were from ASA Grade I & II. The patients were distributed into two groups of 20 each.

Methods and material: Group D (n=20) Patients who received loading dose of Dexmedetomidine 1 microgram/kilogram (µg/kg) over a period of 10 min before induction of anaesthesia and followed by maintenance infusion in the dose of 0.4-0.8 µg/kg/h after intubation via syringe infusion pump. Group N (n=20): Patients who received Inj. Nitroglycerine 5-10 µg/kg/min after intubation via continuous infusion. Patients were monitored for haemodynamic parameters, arterial oxygen saturation and end tidal CO₂ at fifteen minute time interval. Average category scale score was used to assess the Quality of surgical field. Total amount of blood loss was noted.

Statistical test used: Student's t-test

Results: We observed statistically significant increase in mean pulse rate in the Nitroglycerine group as compared to the Dexmedetomidine group. Mean arterial pressure was successfully reduced to the target value in both the groups. There was no difference in amount of blood loss between the two groups.

Conclusions: Dexmedetomidine and Nitroglycerine both can be used with great safety profile to achieve controlled hypotension during FESS.

Keywords: Dexmedetomidine; Nitroglycerine; Controlled hypotension; Functional endoscopic sinus surgery

Introduction

Surgical treatment for chronic infection of nasal and Para nasal sinuses is Functional endoscopic sinus surgery (FESS). Now days, this is a popular technique accepted all over the world due to its minimally invasive nature and there is preservation of mucosa in this technique. However, due to increased vascularity of nasal mucosa, bleeding is the major problem during this surgery. If bleeding is increased, surgeon has to do frequent suctioning in the operative field so as to optimize the field at the cost of prolonging the duration of surgery. Major complications like optic nerve damage, damage to the Dura and even meningitis have been reported for FESS under general as well as local anaesthesia [1,2]. The threat of serious complications resulting from poor visibility and neurological damage associated with hypotensive anaesthesia makes it important for anaesthetists to produce optimal surgical conditions. So the aim should be to reduce blood pressure as little as possible while providing the best possible surgical field. This surgery can be done under local anaesthesia as well as general anaesthesia. General anaesthesia is often chosen over local anaesthesia blocks because there are chances of incomplete block and discomfort to the patient with local anaesthesia whereas in general anaesthesia patients are pain free and additionally various drugs used to produce general anaesthesia also helps in achieving controlled hypotension [3]. Controlled hypotension is the commonly used technique to limit blood loss and improve visualization in the surgical field during FESS surgery. Various techniques have been adopted to achieve controlled hypotension. One of them is use of pharmacological drugs in the form of volatile anaesthetics, direct-acting vasodilators, autonomic ganglion-blockers, α-adrenergic receptor blockers, beta-adrenergic blocking agents, prostaglandin E1, magnesium sulfate and calcium channel blockers [4-10]. Dexmedetomidine is a α₂-adrenoceptor agonist. Literature is not enough to evaluate its effects on lowering the heart rate and mean arterial pressure but still it was considered to be a good agent for producing controlled hypotension [5,11,12]. The main advantages of dexmedetomidine infusion are the absence of reflex tachycardia and no chances of rebound hypertension as the sympathetic nervous system is suppressed [13,14].

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Nitroglycerine is a directly acting vasodilator and it is frequently used to produce controlled hypotension because it is easily treatable and having very rapid onset as well as rapid offset of action. However the disadvantages of nitroglycerine are reflex tachycardia and venous congestion leading to increased blood loss [15].

So, we carried out this study to assess and compare the nitroglycerine (NTG) versus dexmedetomidine infusion in patients undergoing FESS under general anaesthesia with primary objectives being optimization of the surgical field by reducing the amount of blood loss and secondary objectives being monitoring of haemodynamic parameters, time of reversibility of the hypotensive state at the end of surgery and to monitor for any complications.

Method and Materials

Once we got approval from institutional Ethics Committee for Human Research (IECHR) to carry out this study, we included forty adult patients of American Society of Anaesthesiologists (ASA) physical status I and II of both sex having age group between 18-60 years and posted for elective FESS surgery. Our study was a prospective single blind, comparative, randomised, clinical study. We excluded patients having hypertension, Ischaemic heart disease, Patients who had undergone recurrent sinus surgery, Hepatic, renal and cerebral impairment, patients with known Coagulopathies, Patients with heart block, patients having history of allergy to the study drug used, Patients on ACE inhibitors, α-2 adrenergic receptor blockers, Calcium channel blockers and beta blockers.

All the patients underwent a thorough pre anaesthetic examination and written and informed consent was taken. Patients were given Tab. Ranitidine 150 mg and Tab. Diazepam 10 mg orally the night before surgery. On the day of surgery, patients were taken to operation theatre. Multipara vital monitor was attached and preoperative baseline pulse rate, blood pressure and oxygen saturation recorded. Two peripheral veins were taken with 18/20 gauze intravenous vein in each arm. All the patients were premedicated with inj. Glycopyrrolate 0.2 mg IV, inj. Ondansetron 4 mg IV, Inj. Fentanyl 1 μg/kg IV and Inj. Midazolam 0.02 mg/kg IV. For Preparation of Dexmedetomidine infusion, we took two ml of Inj. Dexmedetomidine (100 microgram per ml) in 50 ml syringe and diluted with 48 ml of normal saline. Total 50 ml volume was prepared (4 μg/ml). For Preparation of Nitroglycerine infusion, we took two ampoules of nitroglycerine (50 μg/10 ml) in 50 ml syringe and diluted with 40 ml of normal saline. Total 50 ml volume was prepared (1 μg/ml) in a 50 ml syringe [16,17].

With the help of Epi Info software, Patients were randomly divided into two groups by computer generated random numbers. Each group included 20 patients. Patients of Group D received Inj. Dexmedetomidine loading dose 1 μg/kg over a period of 10 min before induction followed by maintenance infusion of 0.4-0.8 μg/kg/h after intubation via syringe infusion pump. Group N received Inj. Nitroglycerine 5-10 μg/kg/min after intubation via syringe infusion pump. Patients were induced with Inj. thiopentone sodium 5-7 mg/kg IV. After giving short acting depolarising muscle relaxant i.e. Inj. suxamethonium 1-15 mg/kg IV and pressor response attenuating agent i.e. Inj. xylocaine 1-1.5 mg/kg IV they were intubated with appropriate size cuffed oral endotracheal tube. In Group D, maintenance infusion dose of dexmedetomidine (0.4-0.8 μg/kg/h) was started immediately after intubation. In Group N, nitroglycerine infusion was started (5-10 μg/kg/min) immediately after intubation. Anaesthesia was maintained with 50:50 Oxygen and nitrous oxide in addition to sevoflurane 2% and Inj. Vecuronium bromide 0.1 mg/kg bolus dose, followed by intermittent dose of 0.02 mg/kg IV. Patients were ventilated to maintain end tidal CO₂ of 30-35 mm of Hg and SPO₂>95%. Oropharyngeal pack was inserted. Thirty (30) degree reverse trendelenberg position was given. Nasal mucosa was infiltrated by epinephrine in a conc. of 1:100000 by Surgeon. Dexmedetomidine/ Nitroglycerine infusion was titrated to maintain MAP between 55-65 mm of Hg (Target MAP). Maximum infusion rate was in Group D 0.8 μg/kg/h and in Group N 10 μg/kg/min. Patients who reached the maximum dose without achieving the target MAP were excluded from our study & they were given inj. esmolol 0.5-1 mg/kg loading dose, followed by infusion if needed to reach to target MAP. Once the target MAP was reached, surgery was allowed to proceed with the surgery. Patients were monitored at 15 min time interval for pulse rate, mean arterial blood pressure, arterial oxygen saturation and end tidal CO₂. Quality of surgical field was assessed by Average Category Scale (adopted from Fromme et al.) [18]. At half hourly interval, once the Target MAP was reached. It is categorised as 0=Absence of bleeding, 1=slight bleeding, suctioning of blood not necessary, 2=slight bleeding, sometimes blood has to be suctioned out, 3=slight bleeding, sometimes blood has to be evacuated, visible operative field for some seconds after evacuation, 4=average bleeding, blood has to be often evacuated, operative field is visible only right after evacuation and 5=high bleeding, constant blood evacuation is needed, sometimes bleeding exceeds evacuation.

We stopped the Dexmedetomidine/Nitroglycerine infusion approximately 20 min before the expected end of surgery. After the stoppage of infusion, Patients were monitored at 2 min time interval for vital parameters especially mean arterial pressure & heart rate. Time was noted for MAP to revert to its baseline level. Approximate amount of blood loss was also noted by calculating the amount of blood collected in suction apparatus and number of soaked gauze pieces. Patients were reversed and extubated after the criteria for extubation were satisfied. Patients were monitored for intraoperative complications in the form of reflex tachycardia and bradycardia. Reflex tachycardia was defined as persistent rise in heart rate>20% from baseline or absolute value of heart rate>120/min for a period of 10 min or more. It was treated with Inj. esmolol 0.5 mg/kg IV. Bradycardia was defined as decrease in heart rate<20% from baseline or<50/min and that was treated with Inj. atropine 0.6 mg IV. They were also monitored for postoperative complications in the form of nausea/vomiting, bradycardia, hypotension and shivering for a period of up to two hours.

Statistical analysis

We calculated the sample size with reference to the study done by Jamal et al. [16] taking the mean values of blood loss in the Dexmedetomidine group and Nitroglycerine group in their study as main parameter. With the help of Medcalc software, considering type-1 (alpha) error as 0.05 and type-2 (beta) error as 0.2, sample size came to be 19 in each group. So we chose to select a sample size of 20 per group. Results were analysed by taking out their mean and standard values and thereby deriving probability (p) values from it. Analysis of variance (ANOVA) for the various parameters was done using student’s paired t-test for intragroup comparison and unpaired t-test for intergroup comparison. P<0.05 was considered as not significant, P<0.05 significant and P<0.01 highly significant.
Results

As shown in Table 1, the two groups in our study were showing no significant difference i.e. they were comparable to each other with respect to demographic data and duration of surgery.

|                      | GROUP- D | GROUP- N | P Value |
|----------------------|----------|----------|---------|
| Age (years) (Mean ± SD) | 31.55 ± 9.372 | 28.90 ± 4.7892 | NS |
| Weight (Kgs) (Mean ± SD) | 59.00 ± 4.7573 | 59.75 ± 5.8117 | NS |
| ASA Grade (I/II)      | 16/4     | 15/5     | NS      |
| Duration Of Surgery (Min) | 122.3 ± 19.02 | 111.8 ± 25.51 | NS |

Table 1: Demographic Data.

As shown in Figure 1, there was significant decrease in pulse rate; 15 min onwards in Group D and that persisted throughout the surgery. Whereas, there was significant increase in pulse rate in Group N starting immediately after intubation and that too persisted throughout the surgical duration. Though it was statistically significant, but clinically insignificant and so need not require any treatment except three cases of reflex tachycardia in Group N, who were treated with inj. esmolol 0.5 mg/kg intravenously.

Figure 1: Changes in mean pulse rate.

As shown in Figure 2, changes in mean arterial pressure (MAP) was successfully reduced to the target value (55-65 mm of Hg) in both groups. Not a single patient in any of the two groups required additional therapy to achieve target MAP.

As shown in Figure 3, Optimum quality of surgical field as indicated by Average category scale (ACS) of 2-3 was attained in both groups; there was no significant difference in between group scores.

Figure 3: Quality of surgical field (Assessed by ACS Score)

There was statistically no significant difference with regard to amount of blood loss between the two groups (Figure 4). Amount of blood loss in Group D was 160.8±28.11 ml and in Group N, it was 168.5±24.12 ml (p>0.05).

Figure 4: Amount of blood loss

As shown in Figure 5, time taken for MAP to return back to normal was significantly lesser in the Group N when compared to the Group D. MAP reverted back to normal within 7.8000 ± 5.1052 minutes in Group D and within 2.6000 ± 1.1425 minutes in Group N. We observed reflex tachycardia in three patients of Group N during the intraoperative period and they were treated with inj. esmolol 0.5 mg/kg intravenously. No post-operative complications were seen in either of the two groups.

Figure 5: Time taken for MAP to return to normal

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Discussion

FESS is a surgical procedure, during which all necessary manipulations are performed while using a fibre optic camera. During the surgery, bleeding has to be minimized, as even a small amount of blood may completely obstruct vision through the endoscope. Various approaches have been used to secure a dry operating field during FESS. Capillary bleeding influences the operative field visibility most and it can be reduced by providing hypotension and using local vasoconstrictors. So for reducing bleeding under general anaesthesia, controlled hypotensive technique is a widely adopted one, which involves deliberately lowering the patient’s mean arterial blood pressure to below normal. Literature is showing the use of various pharmacological agents to produce controlled hypotension in various surgeries [4-10].

As vital organ perfusion as well as tissue perfusion is decided by mean Arterial Pressure (MAP); we decided to choose MAP as a parameter to quantify hypotension [19]. We kept the target MAP between 55-65 mm of Hg in our study. Many investigators studied patients subjected to controlled hypotension. They had kept the target MAP range between 55-65 mm of Hg. When they investigated their hormonal and metabolic responses, there was no risk of tissue ischemia [20]. So we also decided the value of MAP to be kept between 55 and 65 mm of Hg in our study. The studies which targeted their MAP value between 55-65 mm of Hg were those done by Shams et al. [21], Khalifa et al. [22] and Boezaart et al. [3].

Our primary outcome parameters were to assess the visibility of surgical field with the use of Average Category Scale (ACS) Score and also to measure the amount of blood loss. We took the Average Category Scale (ACS) as per reference from Fromme et al. [18] to assess the quality of surgical field. When we achieved the Target MAP of 55-65 mm of Hg in both the groups within our selected infusion dose range, the ACS score between 2 and 3 was achieved. As shown in Figure 1; ACS Scores for a bloodless surgical field were achieved between 2 and 3 in both groups. Khalifa et al. [22] studied three different groups using Dexmedetomidine, magnesium sulphate and Nitroglycerin to provide deliberate hypotension. They were successful in achieving their target MAP between 55-65 mm of Hg. However, they concluded that Dexmedetomidine showed better cardiovascular stability as compared to other two agents. In a prospective randomized study by Shams et al. [21] of dexmedetomidine or esmolol in combination with sevoflurane in FESS found that both drugs were effective in achieving MAP of 55 to 65 mmHg, and ensured bloodless surgical field during FESS. They had predetermined the ACS score to be between 2 and 3 to provide bloodless surgical field and they achieved these score values in their study in both the groups. Gupta et al. [23] carried out a placebo controlled study with Dexmedetomidine infusion. They used Dexmedetomidine along with isoflurane in a concentration so as to lower the blood pressure to 30% below baseline and found out that the patients receiving dexmedetomidine infusion had bloodless surgical field and better visibility when compared to patients receiving placebo. Dexmedetomidine suppresses sympathetic nervous system which results in low blood pressure and reduced heart rate and thereby decreases blood loss at the surgical site to improve the quality of the surgical field [24]. Nitroglycerin releases nitrite ions as a by-product which gets converted to nitric oxide (NO). This nitric oxide activates the guanylyl cyclase enzyme which causes vascular smooth muscle relaxation. So this will dilate the peripheral vessels which will reduce venous return to the heart leading to reduction in cardiac output and eventually leading to hypotension [15].

The amount of blood loss was comparable in both the groups in our study. Our results were in consonance with the results of Gupta et al. [23] who also observed no significant difference in amount of blood loss in dexmedetomidine group, nitroglycerin group as well as magnesium sulphate group. Our results were in contrast with the result of Jamaliya et al. [16]. They observed that amount of blood loss and blood transfusion requirement were significantly higher in NTG group than in DEX group. Actually they carried out this study in spine surgeries and blood loss in spine surgery is mainly dependent on congestion of veins around the vertebral bodies. NTG is a peripheral vasodilator agent with its predominant effect on veins. Dilatation of the venous plexus around the vertebral bodies may have contributed to increased blood loss when NTG was used for controlled hypotension. Durmus et al. [25] have proved in a placebo controlled study that dexmedetomidine decreased bleeding in patients undergoing tympanoplasty and septrhinoplasty.

As shown in Figure 1; patients who received Dexmedetomidine infusion showed cardiovascular stability whereas there was significant tachycardia in Group N which persisted throughout the surgical duration. There was clinically significant increase in pulse rate in three cases in patients who received Nitroglycerin infusion which were treated with inj. esmolol 0.5 mg/kg intravenously. Our results were in consonance with the study done by Jamaliya et al. [16] who also observed that NTG group showed a mean rise in heart rate by 28.46% from baseline values as compared to the DEX group which showed a mean fall in heart rate by 21.7%. Khalifa et al. [22] studied three different groups; Gr. D, Gr. M and Gr. G receiving dexmedetomidine, magnesium sulphate and nitroglycerin respectively. They also found similar results in the form of significant decrease in heart rate in Gr. D where as significant increase in heart rate in Gr. G (NTG) during the period of observation. Underlying mechanism for tachycardia with nitroglycerine infusion is activation of renin angiotensin system. Nitroglycerine is also known to cause reflex tachycardia [26,27].

We also observed time to reversion of hypotensive state at the end of operation as our secondary outcome parameters. As shown in Figure 5, time to reversion of the hypotensive state was significantly lesser in the Group N when compared to the Group D. Patients in Dexmedetomidine group were cardistable at the time of extubation. Nitroglycerin has a half-life of one and a half minute only. NTG produces its hypotensive action by liberating nitric oxide (NO) which is having ultra-short half-life of just 0.1 s [28]. Dexmedetomidine acts by selectively binding to a2 receptors with great affinity. So, the hypotension in DEX group can be reverted only when the drug diffuses...
out of its receptors [29]. This could explain our findings, which is in agreement with those of study done by Jamaliya et al. [16]. None of the patients in either of the two groups had any complications like clinically significant bradycardia, hypotension, nausea/vomiting and shivering in the postoperative period. In other studies too, no significant postoperative complications were noted in patients receiving either dexmedetomidine or nitroglycerine infusion for controlled hypotension.

Our study did not assess the analgesic and sedative effects of Dexmedetomidine from statistical point of view. Though practically first requirement of analgesics was delayed in group D in most of the cases. Even we did not assess the discharge time from PACU. We will try to include these parameters in future large scale studies. Here we mainly concentrated on controlled hypertensive effects of these two study drugs. Limitation of this study was lack of bispectral index monitoring to assess the depth of anaesthesia. We did not take control group as it would be unethical not to control bleeding during surgery. Cardiac output monitoring could not be assessed due to limited resources in our institute.

Thus we can conclude that both Dexmedetomidine and Nitroglycerine are safe agents for controlled hypotension and are effective in providing ideal surgical field during FESS. However, Dexmedetomidine has an added advantage of maintaining better cardiovascular stability as compared to Nitroglycerine.

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