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Comparative Study of Nitroglycerin and Dexmedetomidine in Patients Undergoing Endoscopic Resection of Nasopharyngeal Fibroangioma

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Abstract

Introduction: Nasopharyngeal Fibroangioma (NPF) is a rare, benign, but locally invasive tumor removed with nasal endoscopy which is minimally invasive and provides a magnified view of the tumor. Hypotensive anaesthesia technique is required to assist in decreasing blood loss and providing bloodless clear field to facilitate surgery. *Aim:* To compare Nitroglycerin and Dexmedetomidine groups for hypotensive anaesthesia in patients undergoing endoscopic resection of Nasopharyngeal Fibroangioma. *Materials and Methods:* This is a prospective, randomized, single blinded study conducted on 40 patients between the age group of 10-20 years undergoing endoscopic resection of Nasopharyngeal Fibroangioma. The patients were randomly divided into two groups of 20 patients each. Group D – Patients who received 'Dexmedetomidine' Group N – Patients who received 'Nitroglycerin'. *Results:* There was no statistically significant difference between the two groups regarding mean arterial pressures. There was statistically significant difference between the two drug groups regarding pulse rate. The mean pulse rate in Dexmedetomidine group was significantly less than in Nitroglycerin group. The average blood loss was more with Nitroglycerin when compared to Dexmedetomidine. *Conclusion:* Nitroglycerine and Dexmedetomidine can be used safely for maintaining hypotensive anaesthesia to achieve the target mean arterial pressure around 60-70 mm/Hg. The blood loss was significantly less in Dexmedetomidine group. Dexmedetomidine was superior to Nitroglycerin in reducing blood loss during the resection.

Keywords: Dexmedetomidine; Nitroglycerin; Nasopharyngeal Fibroangioma.

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Introduction

Nasopharyngeal Fibroangioma (NPF) is a rare, benign, but locally invasive tumor, with an incidence of 1:150000, almost exclusively encountered in the adolescent males [1]. Surgery is considered to be the gold standard treatment. These are enormously vascular tumors and open surgical resection is associated with significant blood loss and postoperative morbidity. Recently, endoscopic excision has been widely employed for the excision of small and medium sized angiofibromas. Nasal endoscopy is minimally invasive and provides a magnified view of the tumor. It is also associated with less postoperative morbidity and low recurrence rate [2]. The major problem with endoscopic surgery is that even minimal bleeding can interfere with endoscopic

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vision. Thus, hypotensive anaesthesia is required to assist in decreasing blood loss and providing a bloodless clear field to facilitate surgery. Controlled (deliberate/induced) hypotension is a technique wherein the arterial blood pressure is lowered in a deliberate but controllable mannerto minimize surgical blood loss and enhance the operative fieldvisibility [3]. There are several pharmacological and non-pharmacological techniques for inducing hypotension. The various pharmacological interventions include volatile anaesthetics, direct-acting vasodilator drugs, ganglion blocking drugs, alpha blockers, beta blockers, combined alpha and beta blockers, calcium channel blockers, propofol, magnesium sulphate, alpha-2 agonists, prostaglandins, tranexamic acid etc. [4]. Nitroglycerin is a direct acting peripheral vasodilator, which primarily dilates capacitance vessels, reducing venous return with concomitant reduction in stroke volume and cardiac output. Dexmedetomidine is an α2 adrenergic receptor agonist causes controlled hypotension by its centraland peripheral sympatholytic action, results in decrease in blood pressure [5]. Hence the present study is undertaken to compare Nitroglycerinvs. Dexmedetomidine infusion for hypotensive anaesthesia in endoscopic resection of Nasopharyngeal Fibroangioma.

Materials and Methods

This is a prospective, randomized, single blinded study conducted on 40 patients between the age group of 10-20 years undergoing endoscopic resection of Nasopharyngeal Fibroangioma in Government ENT Hospital, Osmania Medical College, Hyderabad. After approval by the institutional ethical committee, written informed consent was obtained from the patients during the pre-anaesthetic evaluation. Result values were recorded using a presetproforma.

Inclusion Criteria: ASA Grade I or II, Aged between 10–20 years

Exclusion Criteria: ASA Grade III and IV, Coagulopathy or on Anti-coagulation, with known End – Organ damage, History of known drug allergy to any of the drugs used in this study.

Investigations done: CBC, BT, CT, Blood grouping and typing, Random Blood sugar, Serum Urea and Serum Creatinine, Chest X-Ray, ECG, HIV, HBsAg. Patients included in this study were randomly assigned to receive either Dexmedetomidine (Group D, n=20) or Nitroglycerin (Group N, n=20). In the operating room, following monitors were used as Pulse Oximetry, Blood Pressure cuff for non-invasive blood pressure monitoring, 5 lead ECG, $EtCO_2$ (after intubation). Two cannulas were inserted, one for infusion of Dexmedetomidine or Nitroglycerin infusion and the other for administration of fluids and other drugs. A urinary catheter was inserted.

All the patients were premedicated with Inj. Glycopyrrolate 0.04 mg/Kg, Inj. Ondansetron 0.08 mg/ Kg. In Group- D an infusion of Dexmedetomidine was made by adding 200 µg (2 ml) of Dexmedetomidine to 100 ml of normal saline, administered in paediatric volumetric IV burette set, making it to a final concentration of 2 µg/ml. The infusion was then started; with a loading dose of 1 µg/kg over 15 min followed by a maintenance infusion at 0.5 µg/kg/hr titrated according to the patients desired target blood pressure (21). In Group- N, patients received fentanyl (2 ug/Kg) before induction followed by an infusion of NTG, made by adding 25 mg (5 ml) of NTG to 100 ml of normal saline, administered in paediatric volumetric IV burette set, making it to final concentration of 250 µg/ml. The infusion was then started at the rate of 0.5 µg/kg/min and titrated in between 0.5-5 µg/kg/min according to the target blood pressure.

Both the study groups received standard anaesthetic technique with Inj. Thiopentone sodium 3-5 mg/ kg titrated to loss of eyelash reflex. Endotracheal intubation was facilitated with Inj. Suxamethonium (1.5 mg/kg) and intubation was done with suitable sized cuffed tube. All the patients were mechanically ventilated with 33:66 O_2/N_2O mixtures and Desflurane 4-6% to maintain $EtCO_2$ within normal range of 30-35 mm/ Hg. Muscle relaxation was continued by Inj. Vecuronium. Respiratory rate (RR) and Tidal Volume (TV) were adjusted according to body weight to maintain normocapnia. Patients received normal saline and dextrose; were placed in a 15^0 Reverse trendelenburg position to improve venous drainage and oro-pharyngeal pack was placed. The MAP was then gradually reduced in both the groups to achieve and maintain the target MAP of 60-70 mm/Hg. Patients who developed severe hypotension (MAP < 55 mmHg) were observed by discontinuation of the hypotensive agents and reducing the concentration of Desflurane. If the MAP did not improve 6mg bolus of mephentermine was given intravenously. If any patients developed bradycardia (<50 bpm) then they received Inj. Atropine 0.6 mg I.V.

Infusion of the hypotensive agent was stopped

10 minutes before the end of surgery. Any residual neuromuscular block was antagonized with Inj. Neostigmine 50 µg/kg & Glycopyrrolate 10 µg/kg. Continuous monitoring was carried out throughout the procedure for heart rate, cardiac rhythm, urine output, MAP, oxygen saturation& $EtCO_2$. The urine output was maintained between 0.5 ml/kg/hr and 1 ml/kg/hr in patients.

Observations

The hemodynamic variables were recorded as pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, preoperatively (baseline parameters & intra-operatively at an interval of every 10 mins until the completion of surgery). After the extubation and full recovery, patients were transferred to the post anaesthesia care unit (PACU). The surgery lasted for 150 mins in almost all the patients, so pulse rate and blood pressures and mean arterial pressures were recorded for this duration.

The Statistical analysis was done using Mean, Standard deviation and Independent t- test (for hemodynamic parameters). All recorded data were entered using MS Excel software and analysed using SPSS 16 version software for determining the statistical significance. p values < 0.05 were considered to be statistically significant.

Results

Table 1: Distribution Patient Characteristics in Study Groups

Groups	N	Mean	Standard Deviation	p Value
Age Distribution				
Group- D	20	15.94	±2.26	0.4373
Group- N	20	15.33	±2.64	
Weight Distribution				
Group D	20	45.29	±9.75	0.8192
Group N	20	45.96	±8.63	

The range of ages was between 10–20 years in both the study groups.

The range of weight was 28–60 Kg in both the study groups.

There was no statistically significant difference (p>0.05) between the two groups in age and weight distributions (Table 1).

There is statistically significant difference between the two groups (p <0.05), when the pulse rates were compared (Fig. 1).

Intraoperatively, there is no statistically significant difference between the two groups (p>0.05), when systolic blood pressures were compared (Fig. 2).

Intraoperatively, there was no statistically significant difference between the two groups (p >0.05), when the diastolic blood pressures were compared (Fig. 3).

Intraoperatively, there was no statistically significant difference between the two groups (p>0.05), when the Mean Arterial Pressures were compared (Fig. 4).

The blood loss was measured as blood volume in suction bottle and amount soaked in swabs. The mean blood loss in Group D was less than the

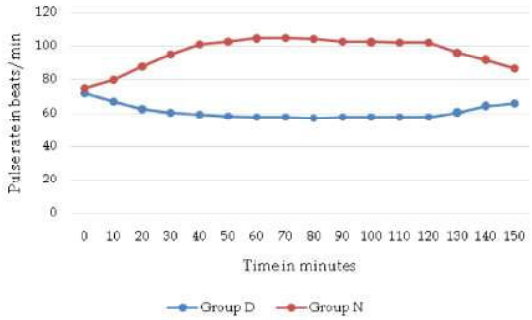

Fig. 1: Hemodynamic Variables Mean Pulse Rates Between Study Groups

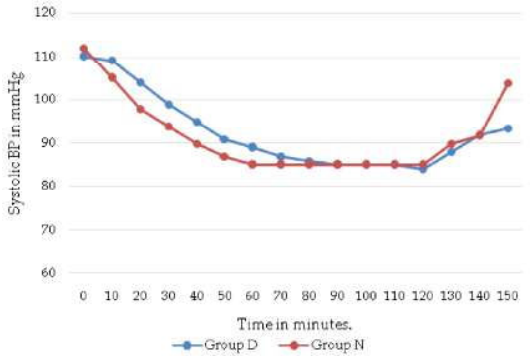

Fig. 2: Mean Systolic Blood Pressure Between Study Groups

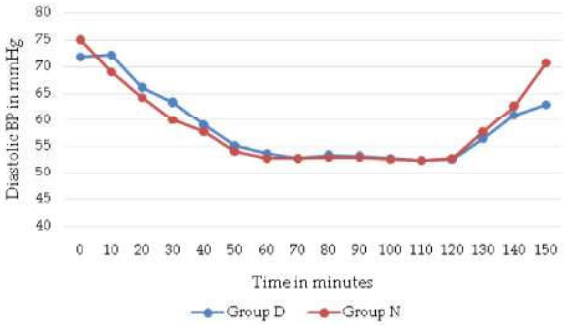

Fig. 3: Mean Diastolic Blood Pressure Between Study Groups

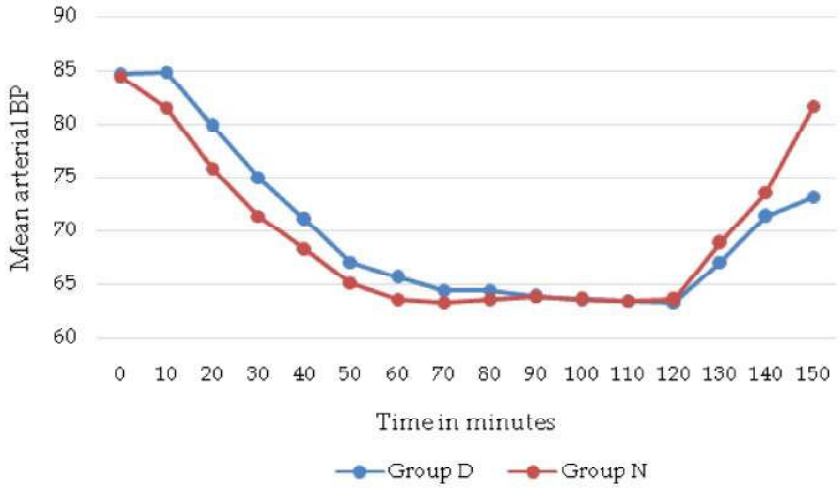

Fig. 4: Mean Arterial Pressure Between Study Groups

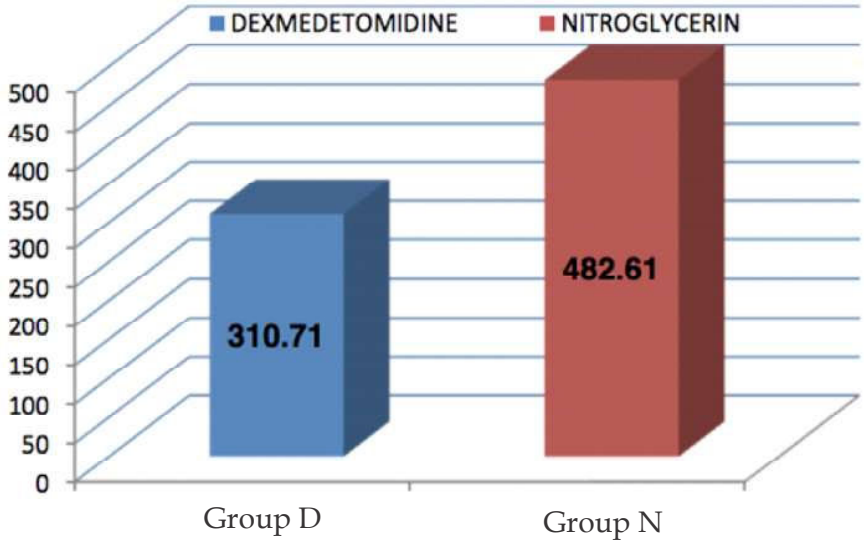

Fig. 5: Mean Blood Loss Between Study Groups

average blood loss in Group N. The difference in blood loss between both the groups was considered to be statistically significant (Fig. 5).

Discussion

Nasopharyngeal Fibroangioma is the most common benign neoplasm of the nasopharynx. It is almost exclusively encountered in adolescent males. They are enormously vascular tumors and open surgical resection is associated with significant blood loss and postoperative morbidity. Recently, endoscopic excision has been widely employed for the excision of angiofibromas. The major problem with endoscopic surgery is that even minimal bleeding can interfere with endoscopic vision. Thus hypotensive anaesthesia is required to assist in decreasing blood loss and providing a bloodless, clear field to facilitate surgery.

Induced or controlled hypotension is a method by which the arterial blood pressure is decreased in a predictable and deliberate manner. The intent of deliberate hypotension is to reduce bleeding and thus facilitate surgery and to decrease the amount of blood transfused.

Care was taken to protect the pressure points by padding. A hypotensive technique reduces the peripheral circulation. This is especially important in areas overlying weight-bearing and bony prominences. Hence, additional supportive pads were placed beneath the patient with special attention paid to the occiput, scapulae, sacrum, elbows and heels. Monitoring of ECG, especially

the V5 lead with ST segment analysis was done to detect cardiac ischemia. Prevention of hypercarbia and hypocapnia are essential in hypotensive anaesthesia. Hypothermia was avoided because it decreases the effectiveness of vasodilators and increases the dose requirements if compensatory vasoconstriction occurs. Proper fluid therapy is essential during hypotensive anaesthesia. The aim of induced hypotension is to lower MAP while maintaining adequate perfusion to all vital organs. Thus, preoperative fluid status was assessed and corrected.

Hypotension was only carried out to that level needed to reduce bleeding and only for that time of the surgery where it is of benefit in reducing significant blood loss. Head end was slightly elevated. Position of the patient is critical to ensure success of the controlled hypotensive technique. Elevation of the site of operation allows easy venous drainage from the site of surgery. This is critical to ensure a bloodless field. But exaggerated head end elevation compromises blood supply to brain during hypotensive anaesthesia, so head end elevation was only limited to 15 degrees.

In this prospective randomized study comparing Dexmedetomidine and Nitroglycerin groups, efforts were made to provide this optimal surgical field. Both the drugs were equally effective in achieving MAP (Mean Arterial Pressure) of 60-70 mm/Hg. The average blood loss was more with Nitroglycerin when compared to Dexmedetomidine. This can be due to increased heart rate & prolongation of bleeding time by NTG due to inhibition of platelet aggregation because similardecrease in mean arterial pressure is achieved by both the drugs. Dexmedetomidine ensured good surgical conditions during endoscopic resection of NPF.

Dexmedetomidine loading dose (1 µg/kg) was given in 15 min before induction of anaesthesia and infusion started after the loading dose. There was significant decrease in MAP and HR. This Dexmedetomidine induced hemodynamic profile can be attributed to the known sympatholytic effect of α2 agonists. The α2-receptors are involved in regulating the autonomic and cardiovascular systems. Alpha 2 receptors are located on blood vessels, where they mediate vasoconstriction on stimulation, and in the brain on sympathetic terminals, where they inhibit, norepinephrine release. At lower doses, the dominant action of α2 agonists is sympatholysis by their central action inhibiting norepinephrine release [23]. Higher doses may cause transient increase in blood pressure due to predominant action on peripheral α2-receptors causing vasoconstriction The efficacy of Dexmedetomidine in providing better surgical field and less blood loss during controlled hypotension was previously reported during tympanoplasty, septoplasty and maxillofacial surgeries as well [24].

Basar et al., [6] investigated the effect of single dose of Dexmedetomidine 0.5 µg/kg administration 10 min before induction of anaesthesia and reported significant reduction in MAP and HR. No other analgesic was used in the Group-D (Dexmedetomidine group); because Dexmedetomidine has inherently got analgesic property due to its action in the locus ceruleus of the brain stem [7,8]. It has been shown to stimulate α2 receptors directly in the spinal cord, thus inhibiting the firing of nociceptive neurons. Even peripheral α2 adrenoceptors may mediate antinociception. No other agent for anxiolysis was also used because Dexmedetomidine has anxiolytic property as well. The efficacy of Dexmedetomidine, in terms of providing an ideal surgical field during control hypotension, was previously reported during middle ear surgery and maxillofacial surgery with predictable hemodynamic effects. The results of the present study showed the same results. The optimal anaesthetic technique to reduce blood loss at the surgical field seems to cause relative bradycardia and associated hypotension.

Ulger et al., [9] compared Dexmedetomidine with Nitroglycerine to achieve controlled hypotension in patients scheduled for middle ear surgery. The infusion rate of drugs was titrated to maintain a mean arterial pressure between 65 and 75 mmHg. They concluded that Dexmedetomidine was better for maintaining hemodynamic stability and a drier surgical field, and was devoid of reflex tachycardia and rebound hypertension. The results of the present study are in accordance with these data.

In the current study, the induction dose of Thiopentone sodium was significantly lower in the Group- D (Dexmedetomidine group) in most of the patients. This effect coinciding with the result of Peden et al., [10] who reported that Dexmedetomidine caused a reduction in the overall dose of induction agent required to produce loss of consciousness. This is because of the sedative and hypnotic properties of Dexmedetomidine.

Guven et al., and Goksu et al., [11,12] reported better hemodynamic stability and visual analog scale pain scores; as well as a clear surgical field and few side effects, with dexmedetomidine infusion in functional endoscopic sinus surgery. In Group-2, Fentanyl 2 ug/Kg was given 3 minutes before induction. Nitroglycerin infusion (0.5-5

ug/Kg/min) was started after induction-intubation.

In the present study, infusion rate was based on the patient's body weight and hemodynamic response and blood pressure was maintained within the range of 60-70 mmHg. Nitroglycerin acts predominantly on venous capacitance vessels, primarily decreases preload to the heart, in addition, it also decreases systemic vascular resistance and afterload. The production of controlled hypotension using this drug depends more on intravascular fluid volume. Excessive decreases in diastolic blood pressure may decrease coronary blood flow. These decreases in diastolic blood pressures may also evoke baroreceptor-mediated reflex increases in sympathetic nervous system activity manifesting as tachycardia and increased myocardial contractility. Nitroglycerin produces a dose-related prolongation of bleeding time that parallels the decrease in blood pressure. It inhibits platelet aggregation. Increased bleeding time could also be the result of vasodilation secondary to a direct effect of Nitroglycerin on vascular tone.

Karl-Erik Karlberg and associates [13] assessed the influence of intravenous Nitroglycerin on platelet aggregation. It was concluded that increasing doses ofintravenous Nitroglycerin profoundly and dose-dependently inhibit platelet aggregation. This inhibitory effect correlates with glyceryl dinitrate formation.

In this study, the mean heart rates in Group-D and Group-N for the entire duration of surgery were 60.61±4.49 & 95.58±9.41 respectively. There was statistically significant difference between the two groups regarding pulse rates. The mean systolic blood pressures in Group-D and Group-N for the entire duration of surgery were 92.73±8.58 & 91.86±8.77 respectively. There was no statistically significant difference between the two groups regarding systolic blood pressures. The mean diastolic blood pressures in Group-D and Group-N for the entire duration of surgery were 58.40±7.03 & 58.33±7.48 respectively. There was no statistically significant difference between the two groups regarding diastolic blood pressures. The mean arterial pressures in Group-D and Group-N for the entire duration of surgery were 69.85±7.47 & 69.54±7.91 respectively. There was no statistically significant difference between the two groups regarding mean arterial pressures. This suggests that both the drug groups are good for achieving controlled hypotensive anaesthesia in endoscopic resection of nasopharyngeal fibroangioma. The mean blood loss in Group-D & Group-N for the entire duration of surgery was 310.71±140.58 ml & 482±141.42 ml respectively.The mean blood loss in Group D was less than the average blood loss in Group N. The difference in blood loss between both the groups was considered to be statistically significant. Infusion of the hypotensive agent was stopped 10 minutes before the anticipated end of surgery. The average blood loss was more with Nitroglycerin when compared to dexmedetomidine. This can be due to increased heart rate caused by Nitroglycerin that is partially offsetting the beneficial effects of hypotension & prolongation of bleeding time by NTG due to inhibition of platelet aggregation because similar decrease in mean arterial pressure was achieved by both the drugs. Dexmedetomidine, on the other hand is an alpha-2 receptor agonist with central sympatholytic action similar to clonidine. This results in decreased in both systemic blood pressure and heart rate.

Conclusion

- Endoscopic removal of Nasopharyngeal Fibroangioma under controlled hypotension technique- Provided a clear field of vision for endoscopic surgery.
- There was no statistically significant difference between the two groups regarding mean arterial pressures.
- Both Nitroglycerine and Dexmedetomidine can be used safely for maintaining hypotensive anaesthesia to achieve a target mean arterial pressure around 60-70 mm/Hg.
- There was statistically significant difference between the two drug groups regarding variations in pulse rate.
- The average blood loss was more with Nitroglycerin when compared to dexmedetomidine.
- Dexmedetomidine is superior to Nitroglycerin in relation to reduction in blood loss during the resection. Dexmedetomidine improved the perioperative hemodynamic stability & causeed controlled hypotension by its central & peripheral sympatholytic action and has got inherent analgesic, sedative and anaesthetic sparing properties which avoids administration of multiple drugs and there side effects.

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