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Original Research Article

Clinical evaluation of efficacy of dexmedetomidine in maintaining intraoperative haemodynamics in posterior fixation surgery following traumatic spine injury

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Abstract

Aim and Objectives: The present study was undertaken to compare the efficacy and safety of dexmedetomidine versus nitroglycerin in maintaining intraoperative haemodynamic stability and postoperative recovery profile in adult patients undergoing posterior fixation surgery for traumatic spine injuries.
Methods: The study enrolling 60 patients of either sex (age 18-50 years), ASA grade I and II were randomly allocated into two groups of thirty patients each. Group DEX received dexmedetomidine 1µg/kg infusion (diluted in 50 ml of 0.9% normal saline) and group NTG received 50 ml of 0.9% normal saline infusion over a period of 10 min as bolus before premedication. The intraoperative haemodynamic parameters, estimated blood loss, operative time, intra and post operative complications, post operative sedation and recovery in patients were noted and compared between two groups.
Results: Dexmedetomidine had better intraoperative haemodynamic stability than nitroglycerine, ($p<0.05$). The mean blood loss and duration of surgery was less with dexmedetomidine than with nitroglycerin, ($p<0.01$). Dexmedetomidine has fewer episodes of complications viz; tachycardia, bradycardia, hypotension and hypertension during and after surgery as compared to nitroglycerin. Post operative sedation was more with dexmedetomidine as compared to nitroglycerin, ($p<0.05$).
Conclusion: Dexmedetomidine is an effective and safe agent in maintaining intraoperative hemodynamics in adults undergoing posterior fixation spine surgery.
Keywords: Dexmedetomidine, Nitroglycerin, Posterior fixation surgery, Traumatic spine injuries

1. Introduction

Significant blood loss during post-traumatic spinal stabilization surgery is a major anesthetic challenge that might require transfusion of whole blood or blood products [1]. The importance of decreasing bleeding in spine surgery is not only important to keep the patient's hemodynamic balance but also allow a better view of surgical field which has the vicinity of major and highly fragile neurologic structures. Improving the surgical field helps the surgeon to decrease the operative time, which further decreases bleeding [2]. In addition to maintaining haemodynamic stability in spine surgeries, it is also desirable to have rapid recovery for early neurological assessment and treatment of

complications. One of the major factors that determine haemodynamic stability and speed of recovery from anaesthesia is the choice of anaesthetic technique. Controlled hypotension is a commonly used technique to limit blood loss and improve visualization of the operative field during spinal fusion surgery [3,4].

Various agents have been used to provide controlled hypotension that include direct acting vasodilators (sodium nitroprusside-nitroglycerin), ganglion-blocking agents, beta adrenergic blockers (esmolol), calcium channel blockers (nicardipine), α_2-agonists (clonidine-dexmedetomidine), and magnesium sulphate [5,6].

Dexmedetomidine (DEX) is a potent and highly selective α2-adrenergic receptor agonist, with a differential affinity for the α_2:α_1 receptors in a ratio 1,620:1. It is a sedative, analgesic, and possesses anaesthetic sparing effect and sympatholytic properties too. The central and peripheral sympatholytic action of DEX are mediated by binding to α_2 adrenergic receptors bringing about dose-dependent decrease in mean arterial blood pressure (MAP), heart rate (HR), cardiac output, and norepinephrine release [7,8].

Nitroglycerin (NTG) a directly acting vasodilator has been used since decades to achieve induced hypotension because of its rapid onset, rapid offset, and titrability. However, it causes reflex tachycardia and venous congestion in and around the surgical site hence causing increased blood loss [9]. The bleeding during operation is mainly of venous origin. Nitroglycerin predominantly dilates venous capacitance vessels causing pooling of blood away from operation site and decreasing blood loss.

Despite several clinical trials that studied the effectiveness of dexmedetomidine in reducing intraoperative bleeding in adults, little is known about its effect in maintaining intraoperative haemodynamics in posterior fixation surgery for spine injuries. Hence, we decided to conduct this prospective, randomized controlled study to compare the efficacy and safety of dexmedetomidine versus nitroglycerin in terms of haemodynamic stability, average blood loss, and operative time, level of sedation and intra and postoperative complications in adult patients undergoing posterior fixation spine surgery.

2. Material and Methods

This was a prospective, randomized double blinded controlled study conducted in the department of anaesthesiology at tertiary care hospital, after obtaining institutional ethics committee approval and written informed consent from all the patients. A total 60 patients of either sex, ASA grade I and II with age between 18-50 years posted for posterior fixation surgery after traumatic spine fractures under general anaesthesia were selected for the study. Patients with ASA grade III and IV, having age < 18 years and > 50 years, emergency patients, patients who had associated co-morbid conditions viz uncontrolled hypertension (HT), uncontrolled diabetes mellitus (DM), Ischemic heart disease (IHD), left bundle branch block (LBBB), Complete heart block, Bypass surgery, Valvular heart disease, history of renal insufficiency, liver impairment or bleeding disorders, patients having known drug allergy and patients with negative response were excluded from the study. The patients were randomized into two equal groups i.e. DEX and NTG groups using a computer-generated set of randomized numbers by using block randomization. Group DEX received dexmedetomidine 1µg/kg infusion (diluted in 50 ml of 0.9% normal saline) while group NTG received 50 ml of 0.9% normal saline infusion over a period of 10 min as bolus before premedication. A detailed pre-anaesthetic evaluation and all relevant investigations were done for all the patients.

After checking and confirming adequate NBM status, patients were shifted to Operation Theatre on stretcher in supine position. On the operation table, IV access was achieved with 18 G intracatheter and intravenous fluid was started. The multipara monitor like ECG, NIBP, SPO_2, $ETCO_2$, temperature probe were applied to the patient and baseline parameters like systolic/diastolic/mean BP, heart rate, SPO_2, along with respiratory rate were recorded. After premedication with ranitidine 50 mg, glycopyrrolate 0.2 mg, midazolam 0.05 mg/kg and pentazocine 0.3mg/kg in both the groups, anesthesia was induced with injection Propofol 2 mg/kg. After checking and confirming bag and mask ventilation, injection vecuronium bromide 0.1 mg/kg was given and flushed. After 3 minutes of mask ventilation endotracheal intubation was done with appropriate size cuffed endotracheal tube. General anaesthesia was maintained on O_2 50%+N_2O 50 % +inhalational Sevofluorane.

The patients were positioned prone on the standard operation table with necessary precautions to protect pressure points and avoid nerve injury and limb ischemia. Patients in the group DEX received a continuous infusion of dexmedetomidine at 0.2-0.5 µg/kg/h, whereas patients in the group NTG received infusion with a nitroglycerine drip (0.01%) at 3- 5 µg/kg/min after positioning. Both the continuous infusions were titrated to achieve the target MAP of 65-70 mmHg prior to skin incision. Both bolus and infusion were given using syringe pump. Adequate muscle relaxation was achieved with incremental doses of injection vecuronium bromide. The same surgical team was chosen

for each surgery to ensure consistency of surgical technique to avoid bias in the study. The amount of blood loss was calculated using gauze piece, swabs, sponges and mop counts and amount of suction minus wash used. If blood loss was above allowable limit, it was replaced accordingly.

The maximum infusion rate in the group DEX was 0.5 µg/kg/h and in the group NTG was 5 µg/kg/min to achieve target MAP of 65-70mmHg. Reflex tachycardia was defined as a persistent increase in HR of more than100 beats per minute (bpm) for a period of 10 min or more. This was treated by IV beta blocker. Persistent bradycardia (HR < 60 bpm) was treated with injection atropine 0.6 mg. Hypotension, defined as MA*P* < 65 mmHg was treated with mephentermine 6 mg. The infusions were stopped immediately after successful placement of the implants and the time taken to restoration of MAP to that of the baseline after stopping of the agent (DEX/NTG) were noted. ET sevoflurane concentration was decreased by 50% at the start of skin closure and turned off at the end of skin closure. Anti-emetic in form of ondansetron (0.1mg/kg) was given at the time of closure. After completion of surgery residual neuromuscular block was reversed with neostigmine (0.05mg/kg) and glycopyrrolate (8ug/kg). The patient's trachea was extubated after meeting extubation criteria and time of extubation was noted.

Haemodynamic stability was assessed by measuring the heart rate and systolic/diastolic blood pressures and mean arterial pressures during the intraoperative period. Average blood loss, duration of surgery and any adverse effects if at all occurred were noted. Post operative sedation score were observed using Ramsay Sedation Assessment Scale at intervals of 5 min up to 30 min.

2.1 Statistical Analysis

Data were statistically described in terms of mean (±SD), frequencies (number of cases) and percentages when appropriate. Data were tested first for normal distribution by Klomogorov– Smirnov test. Comparison of quantitative variables between the study groups was done using Student t test for independent samples if normally distributed. Mann–Whitney U test was used for non-normally distributed quantitative data or Ordinal Data (eg. Sedation score). For comparing categorical data, Chi square test was performed. Exact test was used instead when the expected frequency is less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 21.

3. Observations and results

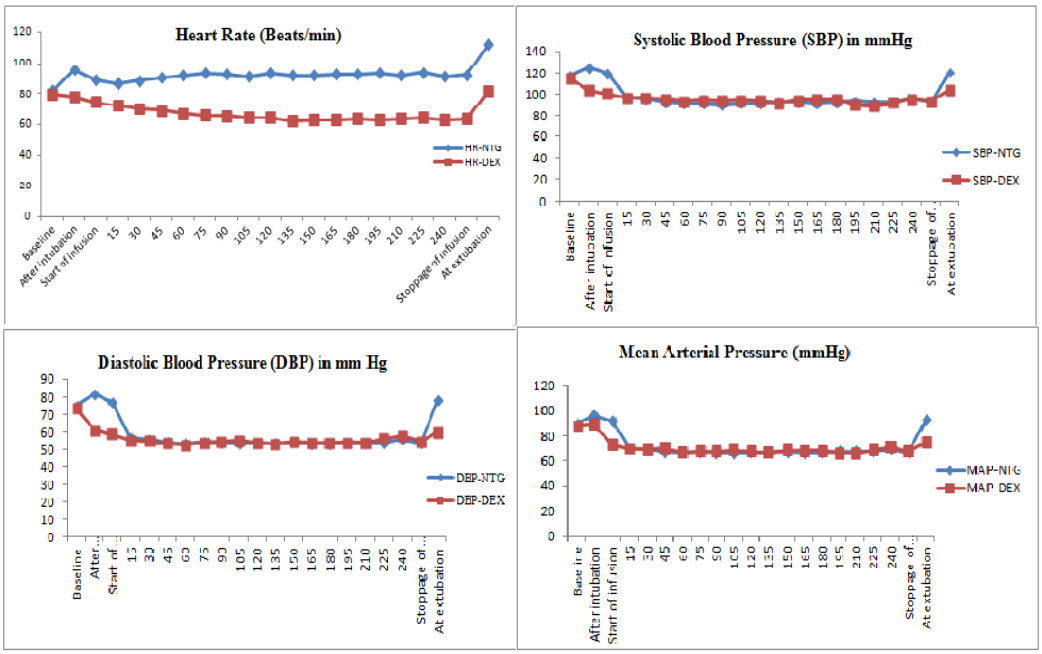
The demographic profiles of the patients were comparable between two groups with regard to age, weight and sex; in both the groups male patients outnumbered the female patients and difference was statistically insignificant. Surgeries in NTG group lasted for longer duration than DEX group. The duration was comparable in both the groups and difference being statistically significant ($p<0.05$), (Table 1).

Table 1: Demographic profile and Duration of surgery

Parameters	Group DEX	Group NTG	P value
Age (years)	40.6 ± 7.7	40.8 ± 8.9	0.939
Weight (kg)	61.0 ± 4.7	58.8 ± 5.1	0.088
Male/Female	24/6	24/6	1.0
Duration of surgery (min)	206.5±16.1	216.0±12.8	0.014

Dexmedetomidine has better control over vital parameters viz; heart rate, mean arterial pressure (MAP), systolic blood pressure (SBP) and diastolic blood pressure (DBP) than nitroglycerine and difference was statistically significant ($p<0.05$). Patients in NTG group had a significantly higher mean heart rate compared to DEX group during the period of observation ($p<0.05$). Thus dexmedetomidine has better intraoperative haemodynamic stability than nitroglycerine, (Figure 1).

Figure 1: Comparison of Haemodynamic Parameters between Two Groups



Arterial oxygen saturation (SpO_2%) between two groups was similar denoting the respiratory and hemodynamic stability with both these agents and difference was statistically not significant. Except at 75 min, 195 min and 210 min where there was statistically significant difference between two groups ($p<0.05$) but these values were within physiological range and none were clinically significant.

Both the groups were similar in terms of episodes of hypotension, hypertension and bradycardia, ($p>0.05$) but patients in NTG group (8 Cases) had more episodes of tachycardia compared to DEX group (1 case) during the period of observation,($p<0.05$), (Table 2).

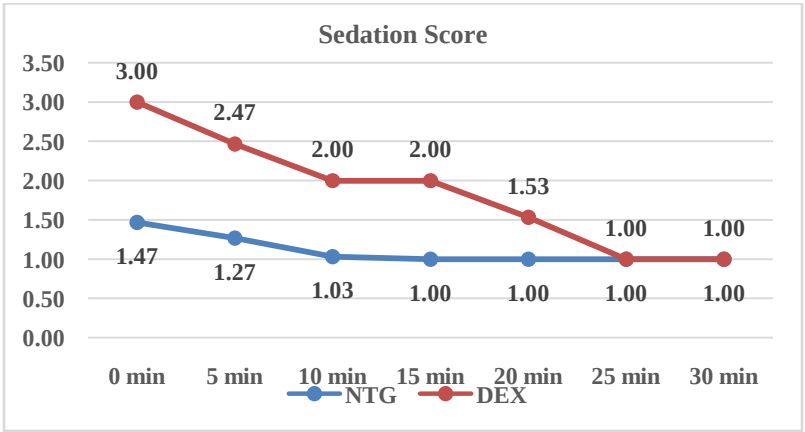
Table 2: Episodes of Complications

Complications	Group NTG	Group DEX	p-value
Bradycardia	0 (0.0%)	2 (6.7%)	0.49
Hypotension	0 (0.0%)	1(3.3%)	1.00
Tachycardia	8 (26.7%)	1 (3.3%)	0.026
Hypertension	2 (6.7%)	2 (6.7%)	1.00

The urine output (ml) during surgery was more in NTG group (495.00±59.23) compared with DEX group (465±41.83), ($P<0.05$). The mean blood loss was significantly lesser in DEX group (426.67 ± 46.86 ml) than the NTG group (605.00 ± 86.45 ml), ($P < 0.01$). The requirement of blood transfusion was significantly more (33.3%) in NTG group than in DEX group (0.0%), ($P < 0.01$).

The sedation score was more in DEX group than NTG group from 5min to 20 min post operative period, ($P < 0.01$) whereas same in both the groups from 25 to 30 min post operative period with no statistically significant difference ($P >0.05$), (Figure 2).

Figure 2: Sedation score between two groups



4. Discussion

Perioperative hemodynamic stability is one of the most important concepts during spine surgery. During surgery, low arterial pressure predisposes patient to spinal cord ischemia, On the other hand abrupt rise in arterial pressure may cause bleeding in the operating field. In adding to hemodynamic stability, rapid and smooth recovery from anaesthesia is also important for immediate neurological assessment in patients undergoing spine surgery. The present study compared the dexmedetomidine and nitroglycerine with respect to their effects on haemodynamic stability, attainment and maintenance of target level of mean arterial pressure, intra operative blood loss, total duration of surgery, intra and post operative complications, post operative sedation and recovery in patients undergoing posterior fixation spine surgery for traumatic spine injury under general anaesthesia. The demographic data of the patients were comparable; this intergroup comparison revealed no statistically significant difference between the two groups and had no influence on outcome of the study. The duration of surgery was less in DEX group in comparison to NTG group which was statistically significant.

Patients in NTG group had a significantly higher mean heart rate (HR) compared to DEX group during the entire period of observation. This shows that dexmedetomidine has greater hemodynamic stability in terms of heart rate than nitroglycerine. Our results were consistent with study of Jamaliya *et al* [10]. There was no statistically significant difference observed in baseline systolic/diastolic/mean arterial pressure amongst two groups. After endotracheal intubation, there was rise in SBP and DBP in NTG group compared to DEX group while at the start of infusion drips, there was fall in SBP/DBP in both the groups and this difference was statistically very significant, (p value < 0.01). SBP from 45 min and DBP from 15 min onwards after start of the infusion drips till 210 min, there was gradual fall in SBP/DBP in both NTG and DEX group noted. This fall in BP was within physiological range and difference was statistically significant, (p value < 0.05). At 225 min after start of the infusion drips, there was rise in SBP/DBP in both the groups, (p value < 0.05). At 240 min after start of the infusion drips and at stoppage of infusion drips, there was rise in DBP in both NTG and DEX group, (p value > 0.05). At extubation SBP in NTG group was 120.60 ± 5.23 and in DEX group was 104.47± 3.43 while DBP in NTG group was 78.20±5.18 and in DEX group was 59.93±3.54, this difference was statistically very significant, (p value < 0.01). After endotracheal intubation there was a rise in MAP while at the start of infusion drips, there was fall in MAP in both the groups, (p value < 0.01). There was fall in MAP in both groups from 45 min onwards after start of the infusion drips till 75 min, this fall in BP was within physiological range, (p value >0.05) while from 15 min onwards after start of the infusion drips till 240 min the MAP was well maintained within required target level in both the groups. At 45, 90, 105, 150, 165,180 and 210 minutes intervals the MAP was well maintained within target level in both NTG and DEX group and difference was found to be statistically significant, (p value < 0.05). However at all remaining specified time intervals viz; 15, 30, 60, 75, 90, 120, 135, 150, 195, 225 and 240 minutes, the MAP was well maintained within target level in both the groups, but difference between two groups was statistically not significant, (p value > 0.05). There was a rise in MAP observed in both the groups at extubation, (p value < 0.01). These observations show that after stopping of both the infusions (30 min before skin closure) the effect of nitroglycerine wears off soon due to short duration of action but due to comparatively longer duration of action of dexmedetomidine the hemodynamic stability was well maintained even during and after extubation period in DEX group patients. Our results regarding haemodynamic stability were correlates with different studies [11-14].

The oxygen saturation variations were comparable between two groups with no statistically significant difference. Except at 75 min, 195 min and 210 min where there was statistically significant difference between two groups (p<0.05) but these values were within physiological range and none were clinically significant.

Hypotension and bradycardia are well known adverse effects of dexmedetomidine. In current study episodes of hypotension and bradycardia between NTG and DEX groups were comparable. In NTG group none of the patients had episodes of hypotension or bradycardia where as in dexmedetomidine group 1 patient had hypotension and 2 patients had bradycardia but which were not statistically significant (p>0.05). The result was compared with previous studies [15-17]. Patients in NTG group (8 Cases) had more episodes of tachycardia compared to DEX group (1 case) during the period of observation whereas both the groups were comparable in terms of episodes of hypertension.

The intraoperative blood loss and blood transfusion requirement were significantly lower in DEX group than in NTG group, this was comparable with the study of Jamaliya *et al* [10]. As the target MAP (65-70 mmHg) was achieved in both groups of the present study, it is conceivable that some degree of venous congestion occurred in the NTG group that resulted in increased blood loss. Although the organic nitrate vasodilators like NTG inhibit platelet function via production of nitric oxide, it is unclear whether this is a contributing factor in the increased blood loss in the NTG group in our study [18].

The sedation score was more in DEX group compared to NTG group from 5 min to 20 min post operative period while it was same in both the groups from 25 to 30 min post operative period with no statistically significant difference (P >0.05). We concluded that patients in DEX group were sedated in immediate post operative period which wears off gradually while less sedation was seen in NTG group. This result compared with the study of Mariappan *et al* [15] and Vanda *et al* [19].

5. Conclusion

From the observations of present study, major inference we made was that dexmedetomidine can be effectively and safely used to achieve and maintain a target level of MAP (hypotension) with the desired hemodynamic stability in posterior fixation surgeries for traumatic spine injuries. This showed a decreased blood loss in the dexmedetomidine group compared to NTG group indicating that the desired level of hypotension was effectively achieved without any adverse effects in intraoperative or postoperative period.

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