



## EVALUATION OF DEXMEDETOMIDINE AND GLYCERYL TRINITRATE AS HYPOTENSIVE AGENT IN SPINE SURGERIES – A CLINICAL STUDY

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### ABSTRACT

**Aim:** Induced or controlled hypotension is a method to minimize bleeding during spine surgeries. This study was designed to evaluate the effect of dexmedetomidine (DEX) as hypotensive agent in spine surgeries as compared to glyceryl trinitrate (GTN). **Subjects and Methods:** 60 patients of either sex of ASA grade I or II in the age group of 18-60 years, undergoing spine surgeries were considered for the study and randomly divided into two groups, with 30 each. (Group I) Dexmedetomidine (DEX) group: was given dexmedetomidine 1 mcg/kg/h over 10 min before induction of anaesthesia followed by 0.2-0.7 mcg/kg/h infusion during maintenance. And (Group II) Glyceryl trinitrate (GTN) group: was given Glyceryl trinitrate 3-5 mcg/kg/min infusion after induction of anaesthesia. **Statistical Analysis Used:** Statistical analysis was done using SPSS and Statistical tests employed were Chi-Square Test and Unpaired Student's t-test. **Results:** Time of recovery from hypotension was significantly higher in GROUP I. Fall in Hct 2hr postoperatively in patients receiving dexmedetomidine was significantly lesser than patients receiving GTN but there was statistically no significant difference in mean Hematocrit value in groups I & II 24hr postoperatively. The MAP showed a significant reduction in DEX group as compared to GTN group but only at three observation times, that is, after induction of anaesthesia, after intubation and at extubation. There was no significant difference noted between the two groups at rest of observation times. The mean Aldrete score at extubation was significantly higher in DEX group. Mean Ramsey Score<sup>[7]</sup> was also significantly higher in DEX group 15 minute Postoperatively but 30 and 60 minute postoperatively, we found no significant difference in mean Ramsey Score. **Conclusions:** Findings of our study conclude that a continuous infusion of Dexmedetomidine is an effective and safe method of producing controlled hypotension in spine surgeries by maintaining better hemodynamics, minimizing blood loss.

**KEYWORDS :** induced hypotension, spine surgeries, Dexmedetomidine , Glyceryl trinitrate

### INTRODUCTION

Spine surgeries are often associated with major blood loss which makes the surgical field visualization difficult and if significant, requires transfusion of blood and/or blood products.

Induced or controlled hypotension is a method by which the arterial blood pressure is decreased in a predictable and deliberate manner (Cushing in 1917)<sup>1</sup>.

The ideal agent for inducing hypotension should have ease of administration, a predictable and dose-dependent effect, rapid onset and recovery from effects, quick elimination without the production of toxic metabolites, and minimal effects on blood flow to vital organs<sup>2</sup>. Although such an agent does not yet exist, many anaesthetic techniques & agents and drugs have been used successfully to produce deliberate hypotension, including

1. spinal and epidural anaesthesia,
2. volatile anaesthetics
3. direct-acting vasodilating drugs (sodium nitroprusside, nitroglycerin, hydralazine, purine derivatives),
4. autonomic ganglion-blocking drugs
5. adrenergic receptor blocking drugs
6. adrenergic receptor blocking drugs
7. combined - and -adrenergic receptor blocking drugs
8. calcium channel entry blocking drugs, and
9. prostaglandin E1 (PGE1)<sup>3</sup>
10. Alpha2agonist (Clonidine and Dexmedetomidine).

Glyceryl trinitrate (GTN) used earlier directly dilates venous capacitance vessels, and used to achieve induced hypotension. However, it causes rebound hypertension & reflex tachycardia and venous congestion in and around the surgical site.<sup>4</sup>

Dexmedetomidine (DEX) is a relatively new drug approved in the year 1999, a potent & selective 2-adrenergic agonist with sympatholytic properties, also been utilized as hypotensive agent during anaesthesia. Dexmedetomidine can limit rebound hypertension and diminish both sympathetic outflow and reflex tachycardia.<sup>5</sup>

This study was designed to evaluate the effect of dexmedetomidine (DEX) as hypotensive agent in spine surgeries as compared to glyceryl trinitrate (GTN).

### MATERIALS & METHODS

Institutional Ethics committee approval and informed consent from the patients were taken for the study.

The study was a prospective cross sectional comparative study done on patients posted for spine surgeries in routine operation hours in the department of Anaesthesiology, Gandhi Medical College and Hamidia Hospital, Bhopal.

#### Inclusion criteria:

1. 18-60 year `s patients of either sex.
2. ASA grade I and II.
3. Cases posted for routine spine surgeries.

#### Exclusion Criteria:

1. Age < 18 years and > 60 years
2. Known case of COPD, asthma
3. Coagulopathy
4. Known Hypertensive or Diabetic patients.
5. Patient with Hypovolemia or Hypotension.
6. Patients with pre-existing cardiac abnormalities.
7. Obese patients (BMI > 30)
8. Allergic to any drug to be used
9. Deranged renal or hepatic function

**METHODS:**

60 patients with equal distribution of 30 each were randomly divided in to:

1. Dexmedetomidine(DEX) group (n=30): was given dexmedetomidine 1 mcg/kg over 10 min before induction of anaesthesia followed by 0.2-0.7 mcg/kg/h infusion during maintenance.

2. Glyceryl trinitrate(GTN) group (n=30): was given Glyceryl trinitrate 3-5 mcg/kg/min infusion after induction of anaesthesia.

After receiving the patient in operating room & securing peripheral venous access using two 18 gauge intravenous (IV) cannulae, basic monitoring were applied. Patients in the DEX group were given 1 mcg/kg infusion (diluted in 50 ml of 0.9% normal saline) over a period of 10 min before premedication.

Premedication with injection glycopyrrolate 0.2 mg IV, injection midazolam 0.05 mg/kg and injection fentanyl 2 mcg/kg in both the groups 3-5 minutes before induction was done. Anaesthesia induction was done with injection propofol 2-3 mg/kg. Endotracheal intubation was facilitated by injection vecuronium bromide 0.1 mg/kg. After placing the patient in prone position, patients in the DEX group were given a continuous infusion of Dexmedetomidine in normal saline at 0.2-0.7 mcg/kg/h, whereas patients in the GTN group were infused Glyceryl trinitrate in normal saline at 3-5 mcg/kg/min through syringe infusion pump. Both the continuous infusions were titrated to maintain the MAP between 65-70 mmHg throughout the surgery.

Anaesthesia was maintained with isoflurane and O<sub>2</sub>:N<sub>2</sub>O (50:50). Isoflurane was kept constant at 1% concentration throughout the period of observation. Adequate muscle relaxation was achieved with incremental doses of injection vecuronium bromide.

The Hb & hematocrit value were obtained for each patient prior to induction and 2hr and 24hr postoperatively.

In both groups, signs of inadequate anaesthesia as increase in the arterial pressure greater than the targeted MAP or somatic responses such as movement, lacrimation or sweating were treated with additional dose of fentanyl 1µg/kg. During intraoperative period, reflex tachycardia was defined as a persistent increase in HR of more than 120 beats per minute (bpm) or more, and hypotension was defined as MAP < 65 mmHg.

The hypotensive infusions were stopped immediately before closure starts and the time to reversibility of the hypotensive state was recorded which is defined as time taken to restoration of MAP to that of the baseline after stopping of hypotensive infusion.

After the surgery, patients were extubated using injection glycopyrrolate 0.01mg/kg IV plus injection neostigmine 0.05mg/kg IV after return of reflexes.

**Observations done:**

- HR
- Systolic Blood Pressure (SBP)
- Diastolic Blood Pressure(DBP)
- MAP
- Plethysmography(SPO<sub>2</sub>),

The above observations were taken at: Before premedication (Ta); immediately after induction(Tb),immediately after intubation (Tc), at the start of the hypotensive infusion (Td) , 15 (T15), 30 (T30), 45 (T45), 60 (T60), 75 (T75), 90 (T90), 105(T105),

and 120 (T120) min after induction; at the point of stoppage of administration of hypotensive infusion (Te), and at extubation (Tf). (T=Time in minutes)

- Haemoglobin Preoperatively And Postoperatively (2hour & 24hour)
- Time of recovery from Hypotension
- Total fentanyl given during surgery

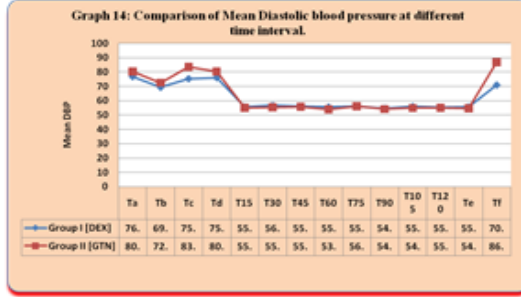
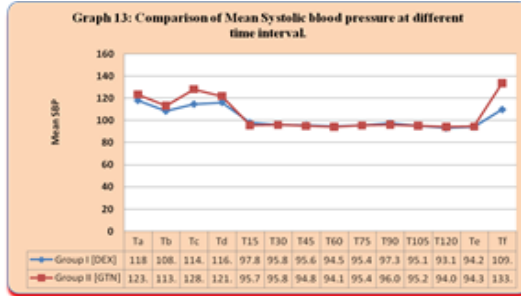
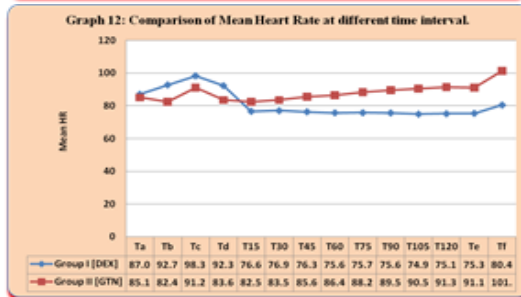
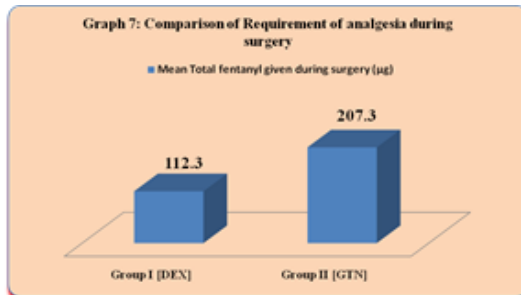
After extubation,patients were transferred to the postanaesthesia care unit (PACU) and observed for Postoperative recovery which is evaluated by using Aldrete score (0-10)[ Aldrete (1995)]<sup>6</sup>. Time to achieve Aldret score of 9 was recorded.

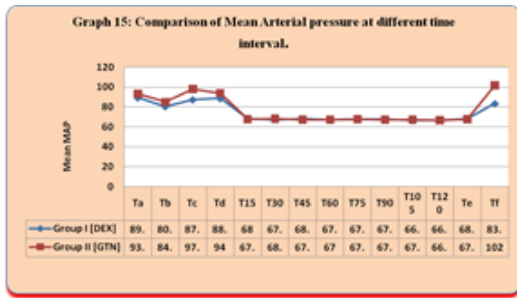
Sedation score [Ramsay, Savage,Simpson et. al.(1947)]<sup>7</sup> was measured at 15, 30 and 60 minutes after tracheal extubation:

**STATISTICAL ANALYSIS:**

Statistical analysis was done using Statistical Package of Social Science). Significance level was fixed at P < 0.05.Statistical tests employed for the obtained data in our study were Chi-Square Test and Unpaired Student's t-test.

**OBSERVATIONS & RESULTS**





**DISCUSSION**

One of the important techniques to reduce bleeding during surgery is by controlled reduction in blood pressure to such levels that the bleeding is minimized without compromising on the perfusion to the vital organs. This is the underlying concept for controlled hypotensive anaesthesia.<sup>[8]</sup>

Reduced bleeding at the operative field gives better visualisation of the surgical site also decreases the handling of tissues thereby reduces iv transfusions and time of surgery.<sup>[9]</sup>

Hypotensive anaesthesia was successfully used in traumatic spine fractures by Ullrich et al<sup>[10]</sup> to reduce blood loss during spine surgeries.

The patients were comparable in relation to the sex distribution age, body weight and duration of surgery( $p > 0.05$ ) and ASA grade.

Preoperative mean Hb & Hct were comparable in between both the groups.

Fall in Hb 2hr postoperatively in patients receiving dexmedetomidine ( $11.873 \pm 1.617$ ) was significantly lesser than patients receiving glyceryl trinitrate ( $11.020 \pm 1.675$ ) ( $p = 0.049$ ) but there was statistically no significant difference in mean hemoglobin 24hr postoperatively between both the groups( $P > 0.05$ ).Jamaliya et al<sup>[11]</sup> found that Dexmedetomidine is effective in minimizing blood loss in posterior fixation spine surgeries and same was reported during middle ear surgeries by Ossama H et. al<sup>[12]</sup> and Tarek Shams et.al<sup>[13]</sup> in FESS

Fall in Hct 2hr postoperatively in patients receiving dexmedetomidine ( $35.70 \pm 4.72$ ) was significantly lesser than patients receiving glyceryl trinitrate ( $33.19 \pm 4.86$ ) ( $p = 0.048$ ) but there was statistically no significant difference in mean Hematocrit value in groups I&II 24hr postoperatively ( $P > 0.05$ ).

Dexmedetomidine, a selective  $\alpha_2$  adrenoceptor agonist, causes fall in blood pressure due to inhibition of central sympathetic outflow and also due to stimulation of presynaptic  $\alpha_2$  adrenoceptors decreasing norepinephrine release.<sup>[14]</sup> While GTN is a direct peripheral vasodilator agent.

Time of recovery from hypotension was significantly higher in group I( $9.00 \pm 1.722$  minutes) as compared to group II( $5.733 \pm 1.68$  minutes)( $p = 0.001$ ).

GTN produces its hypotensive action by liberating nitric oxide (NO) which has a half-life of 0.1 s. DEX acts by selectively binding to  $\alpha_2$  receptors with great affinity.<sup>[15,16]</sup> This could explain the higher time to restoration of baseline MAP in the DEX group compared to the GTN group even after the hypotensive drugs were stopped..

(Graph 7 )The average Fentanyl dose given was significantly higher in Group II ( $207.333 \pm 73.29 \mu\text{g}$ ) as compared to Group I( $112.333 \pm 28.96 \mu\text{g}$ )( $p = 0.001$ ).

In accordance with our results, several studies have demonstrated the analgesic properties of dexmedetomidine<sup>[17,18]</sup>, and significant reduction in the consumption of fentanyl in a dose-dependent manner<sup>[17,18,20]</sup>. This can be explained by central actions in the locus coeruleus and in the dorsal horn of the spinal cord<sup>[19]</sup>.

The mean Aldrete score at extubation was significantly higher in Group I( $7.667 \pm 0.711$ ) as compared to Group II( $7.133 \pm 0.730$ ) ( $p = 0.006$ ).These findings were supported by Ossama H.Aboushanab et.al.<sup>[12]</sup>

15 minute Postoperatively, Mean Ramsey Score[7] was significantly higher in DEX group( $3.733 \pm .449$ ) as compared to GTN group

( $2.833 \pm .37$ )( $p = 0.001$ ). but 30 and 60 minute postoperatively, we found no significant difference in mean Ramsey Score( $p > 0.05$ ).

Due to the higher sedation score observed in the DEX group, earlier discharge from the PACU was recorded in the GTN group. These findings were supported by Ossama H. Aboushanab et.al.<sup>[12]</sup> and Shams T et al<sup>[13]</sup>

The mean HR (Graph 12) was significantly lower in group DEX as compared to group GTN during the period of observation( $P < 0.05$ ). In both the groups, immediately after induction and after intubation ,at the time of extubation ,the mean heart rate was found to be increasing, but this increase in HR was significantly lesser in DEX group as compared to GTN group.

DEX is predominantly sympatholytic so augment cardiac vagal activity resulting in decreased HR and cardiac output.<sup>[17]</sup>

GTN infusion causes activation of the renin-angiotensin system. This may be the cause for increased heart rate in the patients in GTN group during the period of observation<sup>[22]</sup>. Khan and Carleton have cautioned the use of nitroglycerin for induction of hypotension owing to its role in the causation of reflex tachycardia.

(Graph<sup>13,14</sup>) As the infusion of the hypotensive agent was started, a continuous fall in SBP & DBP was noted throughout the infusion in both the groups. In our study we observed that increase in SBP & DBP immediately after intubation and at the time of extubation was significantly lesser in DEX group in comparison to GTN group( $p < 0.05$ ). These findings were consistent with the study by Ossama H. Aboushanab et. al<sup>[12]</sup>, Jamaliya et al<sup>[11]</sup> & Sukhminder Jit Singh Bajwa et al<sup>[22]</sup>

(Graph 15 )The MAP showed a significant reduction in DEX group as compared to GTN group but only at three observation times, that is, after induction of anaesthesia, after intubation and at the time of extubation( $p < 0.05$ ). There was no significant difference noted between the two groups at rest of observation times( $p > 0.05$ ).

In group II, hypotension was seen in 2 patients(3.3%) which were treated with injection Ephedrine 0.1-0.3mg/kg.

This observation suggested that dexmedetomidine is effective in blunting the hemodynamic response of stress during laryngoscopy as has been shown by other studies.<sup>[23,124]</sup>

Cincikas and Ivaskевичius<sup>[25]</sup> used nitroglycerine infusion ( $0.79 \pm 0.34 \text{ g/kg/min}$ ) to maintain MAP of 50-60 mmHg during endoscopic nasal surgery and observed reduced surgical bleeding and improved visualisation of surgical site.

Mean SPO2 was comparable throughout the entire period of

surgery. None of the groups showed hypersensitivity or any side effect.

## CONCLUSION

the findings of our study conclude that a continuous infusion of Dexmedetomidine is an effective and safe method of producing controlled hypotension in spine surgeries by maintaining better hemodynamics, minimizing blood loss, and providing better field of surgery as compared to Glyceryl trinitrate. In addition Dexmedetomidine provides benefit of reducing the analgesic requirements and providing postoperative sedation.

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