Effects of Intravenous Dexmedetomidine on Spinal Anaesthesia with Hyperbaric Bupivacaine

Authors
Shmruthi.S¹, Rajeshwar.P²*, Srinivas.B³

¹Senior Resident, Kamineni Academy of Medical Sciences and Research Centre, L.B. Nagar, Hyderabad
²Associate Professor, Kamineni Academy of Medical Sciences and Research Centre, L.B. Nagar Hyderabad
Consultant Anaesthesiologist, Sunshine Hospitals, Gachibowli, Hyderabad, India
*Corresponding Author
Rajeshwar.P
Email: dr.rajeshwar.kimsrchyd@gmail.com, Mobile no: 9849386578

Abstract
This study was conducted to assess the effects of IV dexmedetomidine on sensory, motor, haemodynamic parameters and sedation during subarachnoid block. 50 ASA I and II patients, aged 18 to 55 years, either sex, scheduled for elective surgeries under spinal anaesthesia, with duration more than 2 hours were included in the study with their informed consent and after approval of research, ethics committee. The patients were randomly allocated into two groups, Group A received IV dexmedetomidine 1mcg/kg bolus over 10 min prior to spinal anaesthesia, followed by an infusion of 0.5 mcg/kg/h for the duration of the surgery. Group B received similar volume of normal saline infusion. Time for the onset of sensory and motor blockade, cephalad level of analgesia and duration of analgesia were noted. Sedation scores using Ramsay Sedation Score (RSS) and haemodynamic parameters were assessed. Demographic parameters, duration and type of surgery were comparable. Significant changes were observed in onset, duration of sensory blockade, two segment regression and duration of motor blockade in Group A while onset of motor blockade was insignificant. There was clinically and statistically significant decrease in heart rate and blood pressures in Group A. The mean intraoperative RSS was higher in Group A. Administration of IV dexmedetomidine during spinal anaesthesia hastens the onset of sensory block and prolongs the duration of sensory and motor block with satisfactory arousable sedation.

Keywords: Dexmedetomidine, intravenous, spinal anaesthesia, supplementation.

Introduction
Subarachnoid block is the preferred anesthetic technique for most of the lower abdominal and lower limb surgeries. It allows the patient to remain awake and minimizes or completely avoids the problem associated with airway management. The technique is simple to perform and the onset of anesthesia is more rapid and reliable than epidural anesthesia.

Lignocaine and hyperbaric Bupivacaine are two commonly used drugs for subarachnoid block. Bupivacaine is three to four times more potent than Lignocaine¹¹ and has longer duration of action. Though the duration of action of Bupivacaine is longer, it will not produce prolonged post-operative analgesia. Achieving high quality postoperative analgesia consistently for a longer time is an attractive goal. One of the methods is addition of an adjuvant to intrathecal Bupivacaine which can
prolong postoperative analgesia. Several additives such as opioids, alpha agonists among others have been used with local anesthetics to prolong the duration of subarachnoid block. Alpha 2 adrenoceptor agonists have been studied as adjuvants to spinal anesthesia with promising results. Clonidine, an $\alpha_2$ adrenergic agonist, has been shown to result in the prolongation of the sensory and motor blockade and the reduction in the amount or the concentration of local anesthetic required to produce post-operative analgesia. Clonidine has been used in various routes like oral, IV, intrathecal to produce prolonged post-operative analgesia[2].

Dexmedetomidine is a more selective alpha 2 adrenocceptor agonist with sedative and analgesic properties. IV dexmedetomidine has been found to reduce the anesthetic requirements during general anesthesia. Dexmedetomidine has been found to exert its analgesic actions both at the spinal and supraspinal levels. A major advantage of dexmedetomidine is its higher selectivity to $\alpha_{2A}$ receptors compared to clonidine which is responsible for hypnotic and analgesic effects5, it has been used safely as premedication or as a sedative agent in patients undergoing surgical procedures under regional anesthesia[3].

There were several studies that compared the use of intrathecal dexmedetomidine in prolonging the duration of spinal anesthesia, very few studies have been done to evaluate its role in prolonging spinal analgesia through intravenous route. Hence we use this intravenous route to determine the prolongation of analgesia by giving dexmedetomidine as a loading dose and continuous infusion throughout the duration of surgery in this present study.

The primary aim of this study was to assess the onset and duration of sensory and motor blockade following IV dexmedetomidine supplementation during subarachnoid block. We also evaluated its effects on haemodynamic parameters, sedation and adverse effects.

Materials & Methods

This study is hospital based, prospective randomised controlled clinical study conducted at Kamineni Academy of Medical Sciences and Research Centre, LB Nagar, Hyderabad during December 2014- August 2015. Fifty patients of ASA-I and ASA-II grade, Age between 18- 55 years and Surgeries more than 2 hours of duration under spinal anaesthesia were included in this study. Patients of ASA class 3-5, Patients receiving calcium channel blockers or ACE inhibitors or clonidine, Patients on sedative medications or opioids or antidepressants, Patients with infection at puncture site, coagulopathies, Patients having true hypersensitivity to Dexmedetomidine, Patients with psychiatric and neurological diseases were excluded from study.

After obtaining institutional ethical approval and a thorough clinical examination and relevant laboratory investigations of all patients, an informed, valid, written consent was obtained, both for conduct of study as well as administration of spinal anaesthesia. All patients were kept nil by mouth from midnight before surgery and tablet Alprazolam 0.5mg was administered at bed time the day before surgery. All the patients were re-examined, assessed pre-operatively on the day of surgery. Intravenous access was established with a 18G intravenous access and preloading was done with 15 ml/kg Lactated Ringer’s solution 30minutes before procedure and baseline parameters were recorded. All the patients were randomly allocated into two groups of 25 each, Group A (dexmedetomidine): bupivacaine and dexmedetomidine group and Group B (Control): bupivacaine and saline group.

Group A patients received a loading dose of 1μg/kg of dexmedetomidine intravenously by infusion pump over 10 mins followed by a maintenance dose of 0.5μg/kg/hr till the end of surgery and Group B patients received an equivalent quantity of normal saline as loading and maintenance dose intravenously by infusion pump and served as control. Immediately after the initial loading dose, under strict aseptic precautions, with the patient in the lateral position, a lumbar puncture is performed at L3-L4 intervertebral space. After ensuring free flow of CSF, subarachnoid block was performed...
with 3 ml of 0.5% hyperbaric bupivacaine. Vitals were recorded (heart rate, blood pressure, SpO2) immediately after the subarachnoid block, considering the time of injection of intrathecal drug as time 0 or the baseline value and every 5 mins for first 15min, for every 15 mins upto 1st one hour of surgical procedure, every 30minutes for next 1hour and every 10minutes for first 30minutes in post anesthesia care unit (PACU).

Sensory blockade was checked with an alcohol swab in mid axillary line. Time taken for the onset of sensory blockade, highest level of sensory blockade and Two dermatomal regression from the maximum level. Sensory blockade was assessed every 2 mins before the onset of surgery and then again postoperatively. All the durations were calculated considering the time of spinal injection as time 0.

Motor blockade was assessed by Modified Bromage Scale. Time taken for motor blockade to reach Modified Bromage Scale 3 and Regression of motor blockade to Modified Bromage Scale 0 were noted. Motor blockade was assessed every 2 mins before the onset of the surgery and every 15 min in PACU. Post-operatively, pain was assessed using visual analogue scale (VAS). The level of sedation was evaluated both intra operatively and post operatively every 15 mins using Ramsay Level of Sedation Scale till the patient is discharged from PACU. Excessive sedation was defined as score greater than 4/6.

Hypotension (systolic blood pressure less than 90 mm Hg or more than 20% fall from baseline value), bradycardia (heart rate <50/min) and postoperative complications like nausea and vomiting were noted and treated appropriately. Patients were given 20 mg/kg (maximum upto 1.2gm) IV paracetamol initially when the patient complained of pain. Diclofenac 75 mg IM was given if patient still complained of pain even after 30 mins after paracetamol infusion. Tramadol 50 mg slow IV was given if patient still complained of pain even at 30 mins after diclofenac administration.

The raw data was entered and mean and standard deviation values were analyzed using Microsoft Office Excel Worksheet 2007 on Microsoft Windows 8 and p-value was analyzed using unpaired t test in Open Epi, Version 3, open source calculator. For statistical significance a p-value of 0.05 or lesser is taken as being statistically significant. Results on continuous measurements are presented as Mean ± SD and results on categorical measurements are presented in Number (%).

Results
This study was carried out on a total number of 50 patients aged between 18-55years of either sex, belonging to ASA class I and II scheduled to undergo elective surgeries under spinal anesthesia. Demographic data, intraoperative and postoperative hemodynamics, motor blockade, sensory blockade, oxygen saturation, Ramsay sedation score, postoperative analgesia and side effects were compared between Dexmedetomidine group (Group A) and Control group (Group B).

There ASA grades, age, sex like demographic data was comparable in both the groups, there was no significant difference between the groups.

The mean duration of surgery in the dexmedetomidine group was 142.8± 21.11 minutes as compared to 158.46± 21.63 minutes in control group and the difference was not statistically significant (P value-0.9061).

Table 1: Type of surgeries in both groups

<table>
<thead>
<tr>
<th>Type of surgeries</th>
<th>GROUP A</th>
<th>GROUP B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopaedic</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Gynaecology</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Gen surgery</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>25</td>
</tr>
</tbody>
</table>

Hemodynamic parameters
The hemodynamic parameters taken into consideration were the heart rate, blood pressure (systolic, diastolic). The results obtained are given below as tables and graphs which compare the mean values of the parameters before and after subarachnoid block. The results are compared within each group and between both the groups before subarachnoid block, at regular intervals after subarachnoid block and till 30 mins after completion of surgery. Various hemodynamic
complications like hypotension, bradycardia are compared in both the groups. The average intraoperative heart rate was significantly lower in dexmedetomidine group [77.2±13.9] as compared to control group [76±6.4] (P value- <0.001), at 60 min. The heart rate was shown in fig 1. The average intraoperative systolic blood pressure (SBP) was lower in dexmedetomidine group [106±12] as compared to control group [108±5.67] (P value-0.0004925) at 30 minutes. Significantly higher number of patients in dexmedetomidine group [7/25- 28%] had lowest SBP >20% of baseline value as compared to control group [2/25- 8%]. The average postoperative SBP was significantly lower in dexmedetomidine group [117±6.14] as compared to control group [132 ±3.45].

There was significant decrease in the diastolic blood pressure in both the groups. The average intraoperative diastolic blood pressure (DBP) was lower in dexmedetomidine group [65.8 ±7.65] as compared to control group [67.5±3.06]. The average postoperative diastolic BP was significantly lower in dexmedetomidine group [117±6.14] as compared to control group [132 ±3.45].

Ramsay sedation score: Intraoperative Ramsay sedation scores were significantly higher in dexmedetomidine group [Mean±SD 4.08 ± 0.95] as compared to control group [Mean±SD 2.32±0.47]. Maximum scores in dexmedetomidine group ranged from 4-6. In dexmedetomidine group maximum sedation score more than 4 was achieved in 52% ofpatients (13/25). Maximum scores in control group ranged from 2-3. Therewas no significant difference in sedation scores between the groups in the postoperative period.

**Duration of sensory and motor blockade:** The duration of motor blockade, duration for 2 dermatomal regression of sensory blockade were significantly prolonged in dexmedetomidine group as compared to control group (P value <0.05). The highest level of sensory blockade was T8 in both the groups. Duration of analgesia and onset of sensory blockade was significantly higher in dexmedetomidine group (P value<0.001). There was no difference in the onset of motor blockade in both the groups. The motor and sensory blockade in both the groups is summarized in Table 2.

<table>
<thead>
<tr>
<th>Table 2: Comparison of sensory and motor blockade in both groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>Highest level of sensory block</td>
</tr>
<tr>
<td>Time for T10 level of sensory block (Onset) in sec</td>
</tr>
<tr>
<td>Onset of motor blockade (MB₃) in mins</td>
</tr>
<tr>
<td>Duration for 2 dermatomal regression of sensory blockade in mins</td>
</tr>
<tr>
<td>Duration of analgesia in mins</td>
</tr>
<tr>
<td>Duration of motor blockade in mins</td>
</tr>
</tbody>
</table>

* indicate Significant change

**Table 3 Comparison of the adverse effects in both groups**

<table>
<thead>
<tr>
<th>Adverse effects</th>
<th>GROUP A</th>
<th>GROUP B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedation</td>
<td>4.08 ± 0.95</td>
<td>2.32 ± 0.47</td>
</tr>
<tr>
<td>Nausea &amp; vomiting</td>
<td>NIL</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>NIL</td>
<td>NIL</td>
</tr>
<tr>
<td>Shivering</td>
<td>2/25(8 %)</td>
<td>5/25(20 %)</td>
</tr>
</tbody>
</table>

**Discussion**

Different drugs like epinephrine, phenylephrine, adenosine, magnesium sulphate, sodium bicarbonate, neostigmine and alpha2 agonists like clonidine, dexmedetomidine have been used as adjuvants to local anesthetics to prolong the duration of spinal anesthesia. Recent studies have shown the efficacy of both intrathecal and intravenous dexmedetomidine in prolonging duration of spinal anesthesia.

**Sensory blockade**

Onset of sensory blockade was significantly faster in group A (96±10) as compared to group B (199±21) p= 0.00055, similar to the study of Harsoor et al. explained that the faster onset may be due to α-2 receptor activation induced inhibition of nociceptive impulse transmission. Although the highest level of sensory block obtained was T8 in both the groups, the duration of sensory blockade and two segment regression were significantly prolonged in dexmedetomidine group. The duration of sensory blockade i.e. time for regression to S1 dermatome was significantly prolonged in dexmedetomidine group [211.28 ± 56.22 min]
compared to control group [156.8 ± 22.95] in our study. Significant prolongation in mean duration of sensory blockade in dexmedetomidine group was also reported by others[4,5,6].

**Figure 1** : Comparison of baseline, intraoperative and postoperative heart rate in both the groups.

![Heart Rate Comparison](chart1.png)

**Figure 2**: Comparison of base line systolic BP and intraoperative Systolic BP

![Systolic BP Comparison](chart2.png)

**Figure 3**: Comparison of the base line systolic BP and post-operative systolic BP

![Systolic BP Comparison](chart3.png)
Motor blockade

In the present study there was no significant difference in time taken for motor blockade to reach modified Bromage Scale 3 in both the groups. However, the regression time to reach the modified Bromage Scale 0 was significantly prolonged in dexmedetomidine group [260 ±35 mins] compared to control group [226 ± 1.54 mins]. Elcicek et al[7] and Hong et al[8] also found that complete resolution of motor blockade was significantly prolonged in dexmedetomidine group.

Effect of dexmedetomidine on heart rate

The intraoperative heart rate was significantly lower in dexmedetomidine group [65.9±6.12] as compared to control group [74±11] at 45 minutes and is similar to Tekin et al[8] study. The lowest mean heart rate after subarachnoid block was significantly lower in dexmedetomidine group [71.8 ± 12.5] as compared to control group [73 ± 7.8] Significantly higher proportion of patients(6) in dexmedetomidine group had bradycardia and is in accordance with other studies[4,5].

Effect of dexmedetomidine on blood pressure

The intraoperative systolic blood pressure (SBP) after spinal block was lower in dexmedetomidine group [105±9.66] as compared to control group [112±6.01] (P value- 0.02381) at 15 minutes. Significantly higher number of patients in dexmedetomidine group [40%] had lowest SBP >20% of baseline value as compared to control group [8%]. The average postoperative SBP was significantly lower in dexmedetomidine group [117±6.14] as compared to control group [132±3.45].

Similarly, the average intraoperative and postoperative diastolic blood pressures were significantly lower in dexmedetomidine group as compared to control group. Previous studies have shown that the hypotensive effect of dexmedetomidine persists in the intraoperative as well as in the postoperative period. Harsoor et al[6] reported minimal decrease in heart rate, blood pressures in patients who received dexmedetom- edine as loading dose was minimal compared to our study. Elcicke et al[7] reported significant decrease in mean arterial pressure after 20, 25, and 30 min after dexmedetomidine infusion as compared to control group. Contrary to above studies and the present study, Al Mustafa et al[5] and Tekin et al[8] reported no significant difference in mean arterial pressures in dexmedetomidine and control groups.In the present study, there was significant difference in the number of patients requiring mephentermine for management of hypotension [40% vs 8% in dexmedetomidine and control groups respectively].

Effect of dexmedetomidine on SpO2

Despite providing good sedation, dexmedetomidine does not cause significant respiratory depression, providing wide safety margins. In our study, there was no significant difference in the oxygen saturation between both the groups during surgery and in the postoperative period similar to the study of Harsoor et al[6], Al Mustafa et al[5] while Hong et al[9] noted desaturation in two patients, attributed to the advanced age of the patients in their study.

Ramsay sedation score

In our study intraoperative Ramsay sedation scores were significantly higher in dexmedetomidine group [Mean-4.08±0.95, Range-4-6] as compared to control group [Mean- 2.32±0.47, Range- 2-3] while in the study of Harsoor et al[6], patients receiving dexmedetomedine were sedated but easily arousable. Al Mustafa et al[5] in their study the maximum score was 5 in 12% of patients, 4 in 79% of patients and 3 in 4% of patients.. Hong et al[9] noted that the median sedation scores during surgery were 4 in the dexmedetomidine group and 2 in the control group.

Postoperative analgesia

Dexmedetomidine inhibits the release of substance P from the dorsal horn of the spinal cord, leading to primary analgesic effects. Dexmedetomidine was found to be effective in providing postoperative analgesia in the present study. The time to first request for postoperative analgesic was significantly prolonged in dexmedetomidine group [211.28 ±56.22 min] as compared to control group [156.8 ± 22.95 min] Kaya et al[10] in their study observed that dexmedetomidine increased the time to first request for postoperative analgesia and decreased analgesic requirements. Whizar-Lugo et al[11] in
their study noticed that the time to first request for postoperative analgesic in dexmedetomidine group was significantly prolonged as compared to control group.

**Postoperative shivering**
Clonidine and dexmedetomidine by inhibition of central thermoregulation and attenuation of hyperadrenergic response to perioperative stress are known to prevent postoperative shivering. In our study, none of the patients in dexmedetomidine group had postoperative shivering as compared to 10% in control group (P value 0.056). Similar results were reported by Harsoor et al\(^\text{[12]}\) (4% and dexmedetomedine and 20% in control group) and Tekin et al\(^\text{[8]}\) (0% vs 30% in dexmedetomidine and control groups respectively).

**Postoperative nausea and vomiting**
No significant difference in the incidence of postoperative nausea and vomiting was noted between both the groups in the present study [4% vs 0% in dexmedetomidine and control groups respectively (P value 0.15)]. Similar results were reported in studies done by Harsoor et al\(^\text{[12]}\), and Al Mustafa et al\(^\text{[5]}\).

**Conclusion**
Intravenous dexmedetomidine significantly prolongs the duration of sensory and motor block of bupivacaine spinal anesthesia. It causes significant decrease in heart rate, systolic and diastolic blood pressures. The incidence of bradycardia is significantly high when intravenous dexmedetomidine is used as an adjuvant to bupivacaine spinal anesthesia, bradycardia, is transient and responds to atropine. The changes in blood pressure are without significant clinical impact and hypotension can be easily managed with bolus of IV fluids and mephentermine. Dexmedetomidine provides excellent sedation during surgery and sedation scores reach normal after stopping the drug and is effective in providing significant postoperative analgesia in first 24 hours and prevents postoperative shivering.

**References**
9. Hong JY, Kim WO, Yoon Y, Choi Y, Kim SH, Kil HK. Effects of intravenous dexmedetomidine on low-dose bupivacaine...