

Intravenous Dexmedetomidine versus Intravenous Clonidine to Prolong Bupivacaine Neuraxial Anaesthesia

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Abstract: Background: Regional (spinal or epidural) or general anesthesia are both alternatives for lower abdominal procedures. However, it has the disadvantages of a shorter block duration and less postoperative analgesia. In an effort to diminish the effects of local anesthetics even more while extending the duration of intraoperative and postoperative analgesia, adjuvants such vasoconstrictors, alpha-2 agonists, and opioids have all been used. Clonidine and Dexmedetomidine, α -2 agonist agents are hypothesized to prolong the effect of spinal anaesthesia when given intravenously. Materials and Methods: This cross sectional study was conducted on 90 patients who were posted for surgical procedures below the umbilicus like abdominal & vaginal hysterectomies, diagnostic laparoscopies, inguinal hernias and lower limb orthopedic surgeries etc. The subjects were divided into 3 groups. Results: There was a significant statistical difference between the groups in terms of mean onset of sensory and motor blocks. (p : 0.01). The onset time was lowest in group A and highest in group C. There was a significant statistical difference between the groups in terms of mean duration of sensory and motor blocks. (p : 0.01). The duration time was highest in group A and lowest in group C. VAS score of group C subjects was highest and group A subjects was the lowest at all intervals. There was a significant statistical difference between the groups in terms of mean rescue analgesics administration time (p : 0.05). The time was highest in group A and lowest in group C. Conclusion: Intravenous dexmedetomidine significantly prolongs duration of sensory, motor blockade and analgesia as compared to clonidine

Keywords: dexmedetomidine, clonidine, spinal anesthesia

1. Introduction

- Spinal anaesthesia or sub-arachnoid block (SAB) involves injection of a local anesthetic into the subarachnoid space.⁽¹⁾
- Spinal anaesthesia is one of the most commonly used techniques in anaesthesia. Major disadvantage of the spinal anaesthesia is short duration of action.⁽²⁾
- Many drugs have been used as adjuvants to local anaesthetic to prolong the duration of action.
- Among these adjuvants; clonidine an alpha2 agonist is widely used by oral and intrathecal routes as an adjuvant to prolong spinal anaesthesia.
- Clonidine, a α 2 adrenergic agonist, has been used widely with spinal anaesthesia to prolong the sensory and motor blockade without significant adverse effects.⁽³⁾
- Dexmedetomidine, a highly selective α 2 adrenergic agonist is reported to have synergistic interaction with local anesthetics.⁽⁴⁾
- The use of intrathecal adjuvants prolongs the duration of spinal anaesthesia⁽⁵⁾. Spinal anaesthesia with or without intrathecal adjuvants is a onetime process. On the other hand intravenous adjuvants can be given continuously as an infusion or as a bolus.

- The duration of surgery can increase due to multiple factors. Intravenous adjuvants can synchronize the duration of surgery with the duration of prolongation of spinal anaesthesia.
- Pain Management is one of the most important part of anaesthesia and its importance is growing as the time progresses.
- Under such circumstances an additive that prolongs the duration of action of a local anaesthetic is an advantage.
- Hence my research focuses on determining the agent that provides maximum duration of analgesia with minimal changes in hemodynamic parameters reducing the requirement of post-operative analgesia

2. Materials and Techniques used

- Patients who are posted for surgical procedures below the umbilicus under spinal anesthesia with ASA grade 1&2 with age 18-60 years, without any premedication drugs are divided into 2 groups.
- Group A (n = 30) will be receiving intravenous dexmedetomidine as a bolus of 1 mcg/Kg over 20 minutes started after the spinal block, followed by 0.5 mcg/kg/h dexmedetomidine drip until end of surgical procedure.

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- Group B (n = 30) will be receiving intravenous clonidine as a bolus of 2 mcg/ kg over 20 minutes, started after the spinal block
- Group C: Subjects managed with a 0.9% saline infusion started after the spinal block (control group)
- The observations made are- Duration of sensory block, Duration of loss of motor block, Ramsay sedation scores, time for first rescue analgesia and hemodynamic changes

Inclusion Criteria

- 1) American Society of anesthesiologists Grade 1 &2
- 2) Age 18 – 60 years
- 3) Patients willing to give consent
- 4) Patients without any premedication drugs

Exclusion Criteria

- 1) Pregnant women
- 2) Chronic medical illness patients
- 3) ASA grade 3 and 4
- 4) Patient allergic to local anesthetics
- 5) Patients going from spinal to general anaesthesia

Statistical plan for evaluating the results:

The data will be analyzed statistically, parametric testing will be done using one-way analysis of variance (ANOVA), intergroup comparison will be done with Tukey’s test and categorical data will be analyzed using the Chi-square test/Fisher’s exact test.

Quantitative Data variables will be given as mean ± SD and Qualitative data variables will be given as (percentage). Mann- Whitney U test will be used to find the group wise comparison for skewed data (Duration of sensory).

The values of P < 0.05 will be considered significant for the study.

3. Results

- The present prospective observational study was conducted on 90 patients admitted in Dr Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinnaoutpally, Gannavaram, Krishna District, in the Department of Anaesthesiology for a period of 24 months (from October 2020 to September 2022). The study population was divided into three groups with 30 subjects each, basing upon the adjuvant used with Bupivacaine.
- Group A: Subjects received intravenous dexmedetomidine as a bolus of 1 mcg/kg over 20 minutes started after the spinal block, followed by 0.5 mcg/kg/ hour dexmedetomidine drip until end of surgical procedure.
- Group B: Subjects received intravenous clonidine as a bolus of 2 mcg/ kg over 20 minutes, started after the spinal block.
- Group C: Subjects managed with a 0.9% saline infusion started after the spinal block (control group).

Table 1: Comparison of Time of onset of sensory and motor block between three groups

Time of onset of sensory and motor block (Minutes)	Group-A Mean ±Sd	Group-B Mean ±Sd	Group-C Mean ±Sd	P- Value
Time of onset of sensory block	4.38 ±1.05	6.08 ±1.15	8.41 ±2.22	0.01
Time of onset of motor block	8.19 ±1.42	10.95 ±2.31	13.53 ±2.85	0.01

- The above table gives data on comparison of time of onset of sensory and motor block between three groups.
- The time of onset of sensory block in groups A, B and C was 4.38 ±1.05 minutes, 6.08 ±1.15 minutes and 8.41 ±2.22 minutes respectively. The statistical P value calculated was **0.01** which indicated that there was a significant statistical difference between the three groups in terms of time of onset of sensory block of the subjects. The time was lowest in group A and highest in group C.
- The time of onset of motor block in groups A, B and C was 8.19 ±1.42 minutes, 10.95 ±2.31 minutes and 13.53 ±2.85 minutes respectively. The statistical P value calculated was **0.01** which indicated that there was a significant statistical difference between the three groups in terms of time of onset of motor block of the subjects. The time was lowest in group A and highest in group C.

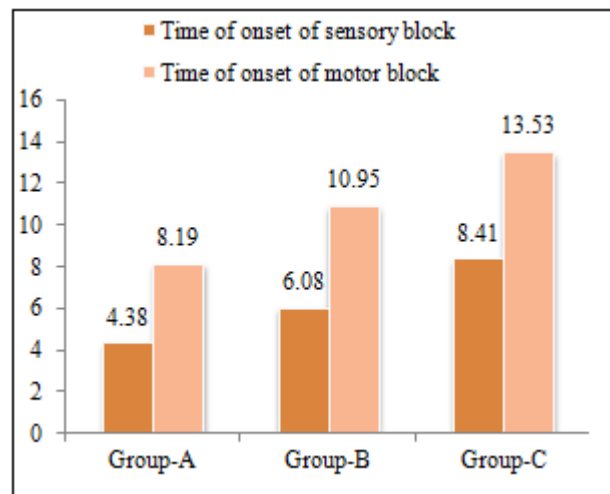


Figure 1: Comparison of Time of onset of sensory and motor block between three groups

Table 2: Comparison of Duration of sensory and motor block between three groups

Duration of sensory and motor block (hours)	Group-A Mean ±Sd	Group-B Mean ±Sd	Group-C Mean ±Sd	P- Value
Duration of sensory block	7.85 ±1.05	7.12 ±1.15	5.35 ±2.22	0.01
Duration of motor block	7.89 ±1.45	7.15 ± 1.13	5.42 ± 2.25	0.01

The above table gives data on comparison of time of duration of sensory and motor block between three groups. The time of duration of sensory block in groups A, B and C was 7.85 ±1.05 hours, 7.12 ±1.15 hours and 5.35 ±2.22 hours respectively. The statistical P value calculated was **0.01** which indicated that there was a significant statistical difference between the three groups in terms of time of duration of sensory block of the subjects. The time was

highest in group A and lowest in group C. The time of duration of motor block in groups A, B and C was 7.89 ± 1.45 hours, 7.15 ± 1.13 hours and 5.42 ± 2.25 hours respectively. The statistical P value calculated was **0.01** which indicated that there was a significant statistical difference between the three groups in terms of time of duration of motor block of the subjects. The time was highest in group A and lowest in group C.

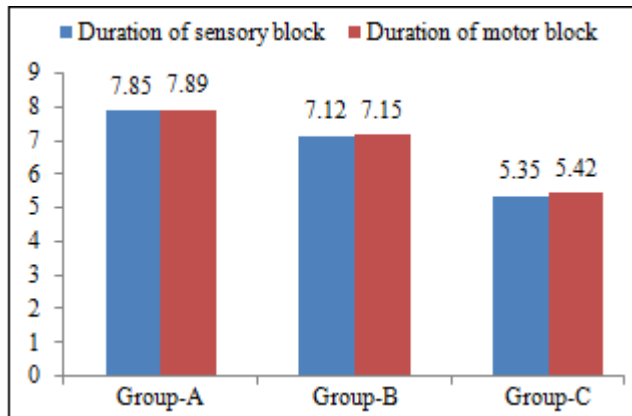


Figure 2: Comparison of Duration of sensory and motor block between three groups

Table 3: Comparison of VAS Score between three groups

VAS Score	Group-A Mean ±Sd	Group-B Mean ±Sd	Group-C Mean ±Sd	P-Value
0 hour	0.63±0.53	1.03±0.87	1.47±0.25	0.01
2 hours	0.87±0.44	1.93±0.78	2.4±0.5	0.01
4 hours	2.23±0.73	2.4±1.67	2.9±0.55	0.001
6 hours	3.57±1.08	3.96±1.63	4.01±0.87	0.05
12 hours	3.23±1.73	3.98±1.73	4.13±0.73	0.05
24 hours	3.67±1.68	3.57±1.81	4.57±0.68	0.05

The above table gives data on comparison of mean visual analogue scale score between the groups.

The mean VAS score of groups A, B and C at 0, 2, 4, 6, 12, 24 hours The p value calculated was **0.05**, indicating a significant statistical difference between the groups in terms of VAS scores of subjects. VAS score of group C subjects was highest and group A subjects was the lowest at 24 hours.

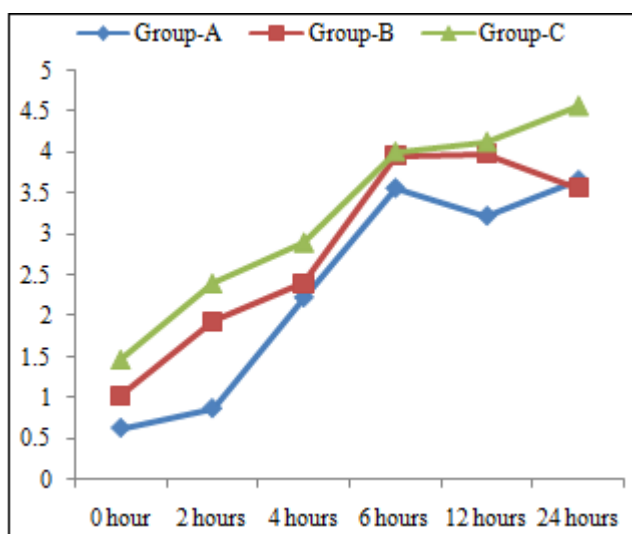


Figure 3: Comparison of VAS Score between three groups

Table 4: Comparison of rescue analgesics between three groups

Rescue analgesics	Group-A Mean ±Sd	Group-B Mean ±Sd	Group-C Mean ±Sd	P-Value
Rescue analgesics	8.38 ±1.46	8 ±1.89	5.30 ±1.18	0.05

The above table gives data on comparison of time of rescue analgesics administration between three groups.

The time of rescue analgesics administration in groups A, B and C was 8.38 ± 1.46 hours, 8 ± 1.89 hours and 5.30 ± 1.18 hours respectively. The statistical P value calculated was **0.05** which indicated that there was a significant statistical difference between the three groups in terms of time of rescue analgesics administration to the subjects. The time was highest in group A and lowest in group C.

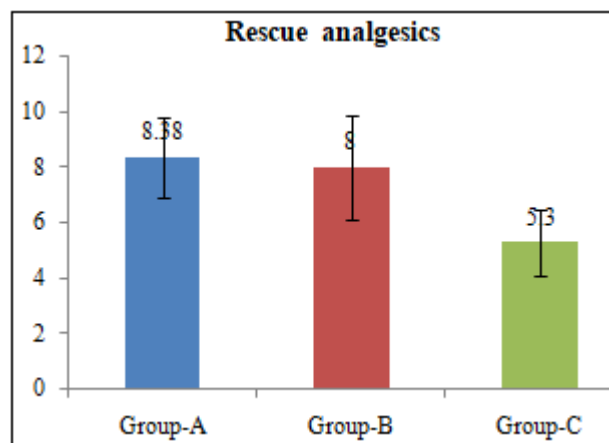


Figure 4: Comparison of rescue analgesics between three groups

Table 5: Comparison of Sedation Score between three groups

Sedation Score	Group-A Mean ±Sd	Group-B Mean ±Sd	Group-C Mean ±Sd	P-Value
Sedation Score	3.61 ± 0.95	2.81 ± 1.69	0.75 ± 0.21	0.09

The above table gives data on comparison of time of Sedation Score between three groups.

The time of Sedation Score in groups A, B and C was 3.61 ± 0.95 , 2.81 ± 1.69 and 0.75 ± 0.21 hours respectively. The statistical P value calculated was **0.09** which indicated that there was no significant statistical difference between the three groups.

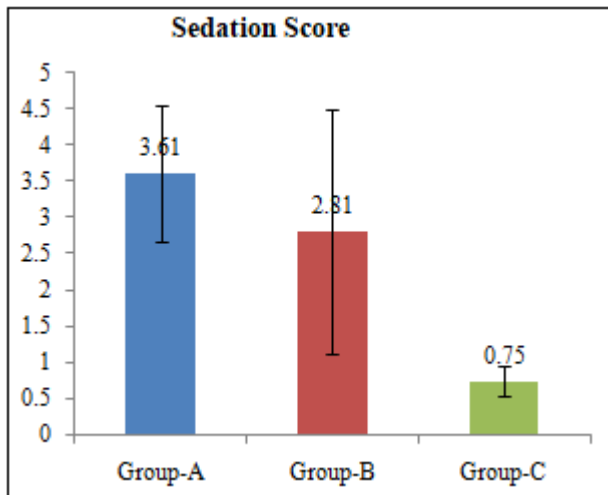


Figure 5: Comparison of Sedation Score between three groups.

4. Discussion

- Alpha2-adrenergic agonists have synergistic action with local anesthetics and may prolong the duration of sensory, motor blockade and postoperative analgesia obtained with spinal anesthesia.
- Many studies have been done using these drugs intrathecally and shown to be effective. The aim of our study was to see the effect of dexmedetomidine and clonidine on spinal anaesthesia by administering them by intravenous route.
- Mechanism of action of dexmedetomidine differs from clonidine as it possess most selective alpha 2-adrenoceptor agonist activity especially for the 2A subtype of this receptor, which causes it to be a much more sedative and analgesic agent than clonidine. Due to this greater selectivity, dexmedetomidine may be more effective than clonidine
- The analgesia produced by α_2 -agonist is due to their action at spinal, supra-spinal, direct analgesic and/or vasoconstricting actions on blood vessels.
- The locus ceruleus and the dorsal raphe nucleus are the important central neural structures where these drugs act to produce sedation and analgesia. This supra-spinal action could explain the prolongation of spinal anesthesia after intravenous administration of dexmedetomidine and clonidine.
- In our study, two-segment regression time of sensory block and time of first request for analgesic were significantly prolonged in the dexmedetomidine group than clonidine. This could be attributed to the mechanism of action of dexmedetomidine which differs from clonidine in being eight to ten times more selective to α_2 -adrenoceptors especially for α_2A and α_2C subtype of this receptor
- Whizar-Lugo et al(5) also found that complete resolution of motor blockade was significantly prolonged in dexmedetomidine and clonidine group. In a study by Kaya et al(6) use of a single dose of 0.5 mcg/kg of dexmedetomidine did not affect the duration of motor block.
- The prolongation of motor block observed in our study may be attributed to the continuous infusion following

the loading dose. It was observed that effect of clonidine on motor blockade was concentration dependent.

- Clonidine directly inhibits conduction large myelinated A alpha fibers and 50% effective concentration measured is 4 fold in small, unmyelinated C fibers. This may lead to relatively less prolongation of motor block than sensory block. The same mechanism is attributable to dexmedetomidine
- Reddy et al(3) also found that dexmedetomidine prolongs duration of analgesia than clonidine
- Hemodynamic parameters, both HR and MAP were stable during perioperative period and the fall in HR and MAP were less than 20% from baseline among the groups.
- The incidence of hypotension and bradycardia were more in the dexmedetomidine group but not statistically significant. These hemodynamic changes were due to decrease in central sympathetic outflow. Similar results were found by Whizar et al (5)& Reddy et al(3)
- The sedation produced by dexmedetomidine differs from other sedatives, as patients may be easily aroused and remain co-operative.
- Reddy et al (3) sedation score greater than 3 and more in dexmedetomidine compared to clonidine.

5. Conclusion

- 1) Duration of sensory, motor blockade and analgesia were statistically prolonged with both intravenous dexmedetomidine and intravenous clonidine.
- 2) Intravenous dexmedetomidine significantly prolongs duration of sensory, motor blockade and analgesia as compared to clonidine

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