*Original Article*

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# Dose Related Prolongation of Hyperbaric Bupivacaine Spinal Anaesthesia By Dexmedetomidine

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**Abstract**

Spinal anaesthesia is commonly used for abdominal and lower limb surgeries. This study has been designed to evaluate the addition of two doses of dexmedetomidine(10µg and 15µg) as an adjuvant to 0.5% hyperbaric bupivacaine 3ml intrathecally for elective abdominal and lower limb surgeries.

***Methods:*** In this randomized, double-blind prospective study, 60 patients of ASA I and II were randomized to three groups: group I, II and III(n=20). All patients received a drug volume of 3.5ml containing 3 ml hyperbaric bupivacaine(15 mg). They received dexmedetomidine 10µg (Group II) or 15 µg (Group III) added to bupivacaine ; the control group (Group I) received 0.5ml of 0.9% saline added to bupivacaine.

***Results:*** It was found that the onset of sensory block upto T10 and motor block is significantly faster in group II (174 sec and 109.5 sec) and III (93 sec and 57.75 sec) over group I (294 sec and 155.25 sec).The mean time for two segment regression and sensory regression to L1, the mean duration of analgesia and motor blockade is significantly prolonged in Group III(138.75 min,469.5 min,438 min,510.5 min) over Group II (104.25 min, 321 min,277.5 min, 323.25 min) and Group II over Group I(88.5 min,257.25 min,238.5 min,265.5 min) ($p<0.001$).

***Conclusion:*** I conclude that 15µg of dexmedetomidine added to local anaesthetic in subarachnoid block has proved to be a better adjuvant in prolonging the sensory and motor blockade and the duration of postoperative analgesia.

**Keywords:** Spinal anaesthesia; Dexmedetomidine; Hyperbaric Bupivacaine; Intrathecal adjuvant; Alpha 2 agonist.

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## Introduction

Spinal anaesthesia is used extensively for lower abdominal and lower extremity surgeries because it has distinct advantages over general anaesthesia, minimum physiological disturbance resulting in minimum stress response, optimal operative conditions, minimal intraoperative blood loss and less postoperative morbidity. Lignocaine and bupivacaine are the commonly used local anaesthetic agents for spinal anaesthesia. Lignocaine produces good motor blockade but duration of action is shorter and is associated with transient neurological complications whereas bupivacaine has been found to have less effective motor blockade but a slower onset of action.[1,11]

Fear of postsurgical pain is a major concern for patients undergoing surgery. Adjuvants are drugs that increase the efficacy or potency of other drugs when given concurrently. Neuraxial adjuvants are used to improve or prolong analgesia and decrease the adverse effects associated with high doses of a single local anaesthetic agent. In addition to their dose sparing effects, neuraxial adjuvants are also utilised to increase the speed of onset of neural blockade (reduce latency), improve the quality and prolong the duration of neural blockade. Neuraxial adjuvants include opioids, sodium bicarbonate ($NaHCO_3$), vasoconstrictors, alpha-2 adrenoceptor agonists, cholinergic agonists, N-methyl-d-aspartate (NMDA) antagonists and γ-aminobutyric acid (GABA) receptor agonists.[5]

Subarachnoid administration of clonidine has been shown to significantly increase the duration of anaesthesia produced by isobaric or hyperbaric bupivacaine with bradycardia, hypotension, arrhythmias, dry mouth as its side effects. Dexmedetomidine is a more selective α2-adrenoreceptor agonist that has been recently evaluated as an adjuvant to intrathecal local anaesthesia.[2,3,10] Based on previous animal[4,9] and human.[3] studies that suggested a 1:10 dose ratio between intrathecal dexmedetomidine and clonidine, we have conducted the study with 10 µg and 15 µg dexmedetomidine as adjuvant to intrathecal bupivacaine.

## Materials and Methods

This prospective double blinded randomized study was conducted in 60 adult patients of ASA grade I and grade II, scheduled for elective abdominal and lower limb surgeries. This study was approved by the Institutional Ethical Committee and written and informed consent was obtained from all the patients before being included in the study.

Patients belonging to ASA grade III, IV and V, with liver and renal dysfunction, cardiac dysarrhythmias, weight >120 kg or height < 150 cm were excluded from the study. Patients concomittantly using adrenergic receptor blockers, calcium channel blockers, with any contraindications for spinal anaesthesia were also excluded from the study.

The patients were randomly divided into 3 groups. Group I received 3.0 ml of 0.5% hyperbaric bupivacaine plus 0.5ml saline. Group II received 3.0 ml of hyperbaric bupivacaine with 10 µg of Dexmedetomidine in 0.5ml Saline. Group III received 3.0 ml of hyperbaric bupivacaine with 15 µg Dexmedetomidine in 0.5ml Saline.

Patients included in the study underwent thorough pre operative evaluation and had basic investigations done which included-Haemoglobin, PCV, Total leukocyte count, Platelet count, BT, CT, LFT, RFT, random blood sugar, ECG, CXR(PA), Blood grouping and cross matching.

In the O.T, appropriate equipment for airway management and emergency drugs were kept ready. The horizontal position of the operating table was checked and patient shifted to the table. 18G i.v cannula was inserted and the patient was preloaded with 500ml of Lactated Ringer's solution. NIBP, $SpO_2$, ECG leads were connected to the patient. Preoperative baseline systolic and diastolic BP, PR, $SpO_2$ and RR were recorded. Under strict aseptic precautions, a midline lumbar puncture was performed using a 25G Quincke needle in sitting position. The patient was then immediately placed in supine position. The time for intrathecal injection was considered as 0 and the following parameters were observed.

- Sensory block was assessed by loss of sensation to pinprick using 23G sterile needle. The assessment was started immediately after injection and continued every 15 sec till loss of pinprick sensation at T10 level. Onset of sensory block was taken as time from intrathecal injection to loss of pinprick sensation at T10. At 20mins interval after SAB, the dermatomal level of sensory block noted and this was considered as maximum level of sensory block.
- Motor block was assessed using Bromage score. Assessment of motor block was started immediately after the intrathecal injection. It was tested every 15 sec till Bromage Score of 4 was reached. Onset of motor block was taken as time taken to achieve Bromage score of 2 from subarachnoid block. The degree

of motor block after 20 min of injection was noted and this was considered maximum degree of motor block. There after, motor block regression was noted and duration of motor block was taken as time from initiation of SAB to return of Bromage Score to 1.

- The PR, systolic and diastolic BP, SpO2 and RR were recorded every 2 min for 10mins and then every 5 mins throughout the intraoperative period. The above vital signs at the completion of surgery were noted. Hypotension was defined as fall in systolic BP > 30 % from baseline or MAP <60mm Hg. This was managed with i.v Mephentermine 6mg in increments. Bradycardia was defined as HR<60/min and was managed with Inj.atropine 0.01mg/kg i.v. Respiratory depression was defined as RR< 8/min and or SpO2 <85%.This was planned to be managed with bag and mask ventilation or intubation and IPPV if necessary. Blood loss more than the allowable loss was replaced with blood.
- The occurrence of sedation was assessed using Ramsay sedation scale.
- At the end of surgery, the degree of pain was assessed using VAS scale till VAS score >4 was reached. Whenever the patient complained of pain,the rescue analgesic Inj. Diclofenac 75mg i.m was given. Duration of effective analgesia was defined as time interval between onset of SAB and the time to reach VAS ≥4 (figure 1).

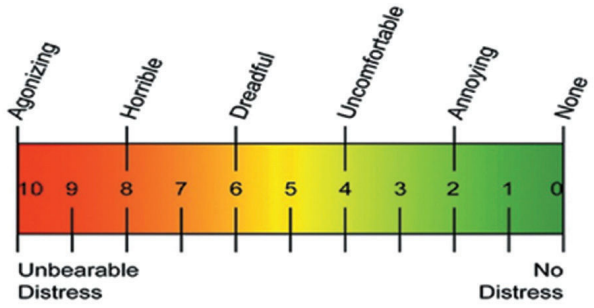



**Fig. 1:** Visual Analogue Scale.

Patient was shifted to recovery room after completion of surgery. The vital signs were recorded, every 15 min in the 1st hour after surgery and 30 min interval for next 2 hours and thereafter at hourly intervals for next 3hrs. Sensory and motor block assessment were done every 15 min till recovery of pin prick sensation to L1 and Bromage score of 1 respectively. Patients were shifted to post operative ward after complete resolution of motor blockade.

Patients were monitored for 24 hours to detect the occurence of side effects respiratory depression, nausea, vomiting, dry mouth and pruritis. Patients were also enquired about the occurence of transient neurological symptoms which was described as pain/paraesthesia in the neck, buttocks, legs or pain radiating to lower extremities after initial recovery from SAB within 72 hrs.

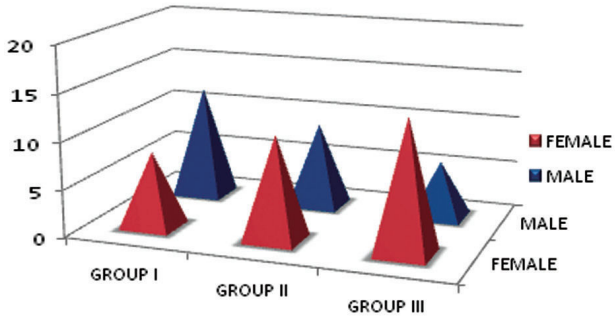
Statistical analysis was done using Median, Analysis of Variance, Chi-square test with Yates correction. The p-value <0.05 was considered significant and a p-value < 0.001 was considered to be highly significant.

## Results

All three groups were comparable and no significant difference was found respect to their gender, age, height, weight, mean duration of surgery (Table 1, Table 2, Table 3, Table 4, Table 5).

**Table 1:** Distribution of sex by groups.

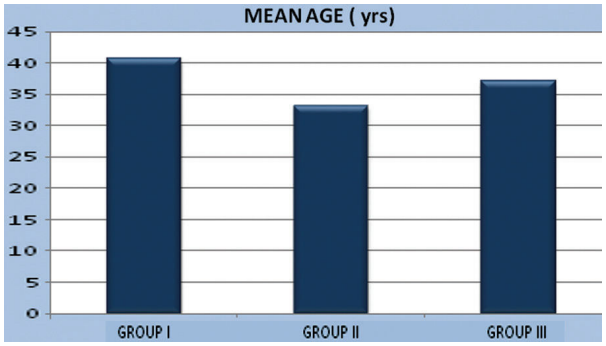
| Gender | Group I | Group II | Group III | p value |
|---|---|---|---|---|
| Female | 8 | 11 | 14 | 0.162 |
| Male | 12 | 9 | 6 | |
| Total | 20 | 20 | 20 | |




**Graph 1:** Distribution of sex by groups.

**Table 2:** Distribution of mean age by groups.

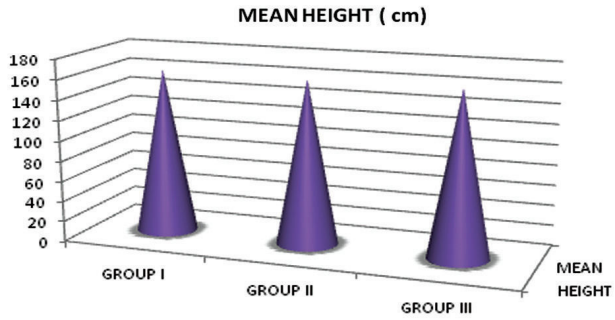
| Age | Group I | Group II | Group III | p value |
|---|---|---|---|---|
| No. of Cases | 20 | 20 | 20 | 0.105 |
| Mean | 40.6 | 33.2 | 37 | |
| SD | 13.57 | 10.19 | 10.83 | |




Graph 2: Distribution of mean age by groups.

**Table 3 :** Distribution of mean height (cm) by groups.

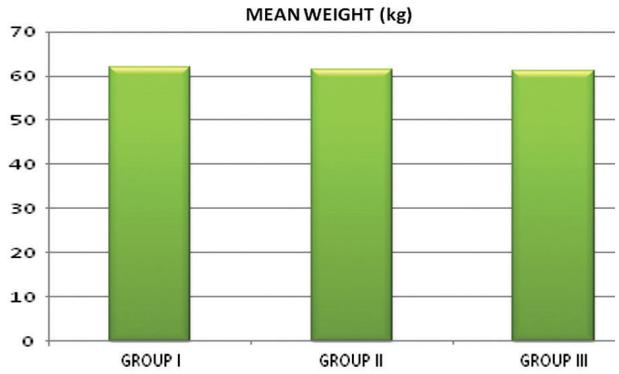
| Height | Group I | Group II | Group III | p value |
|---|---|---|---|---|
| No. of Cases | 20 | 20 | 20 | |
| Mean | 162.95 | 162.25 | 163.05 | 0.905 |
| SD | 6.72 | 5.856 | 5.86 | |




**Graph 3 :** Distribution of mean height (cm) by groups.

**Table 4** : Distribution of mean weight (kg) by groups.

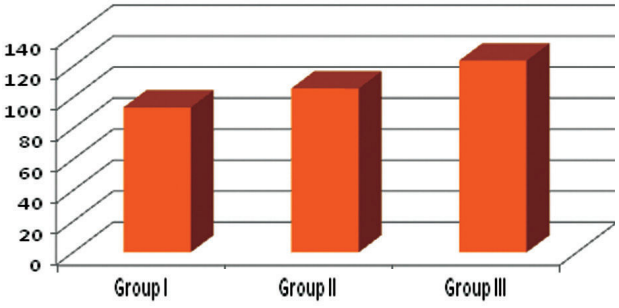
| Weight | Group I | Group II | Group III | p value |
|---|---|---|---|---|
| No. of Cases | 20 | 20 | 20 | |
| Mean | 61.85 | 61.4 | 61.2 | 0.948 |
| SD | 6.93 | 6.94 | 5.33 | |




**Graph 4 :** Distribution of mean weight (kg) by groups.

**Table 5:** Duration of surgery (min).

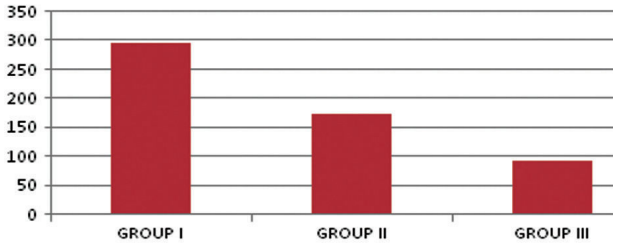
| Duration of Surgery | Group I | Group II | Group III | p value |
|---|---|---|---|---|
| No. of Cases | 20 | 20 | 20 | |
| Mean | 93.5 | 105.75 | 123.75 | 0.58 |
| SD | 40.10 | 41.99 | 35.05 | |




**Graph 5:** Duration of surgery (min).

**Table 6:** Distribution of mean onset of sensory block.

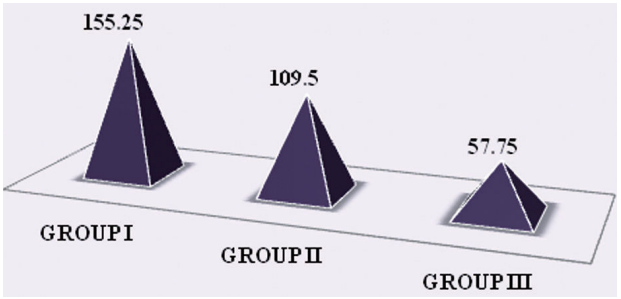
| Onset of Sensory Block | Group I | Group II | Group III | p value |
|---|---|---|---|---|
| No. of Cases | 20 | 20 | 20 | |
| Mean | 294.75 | 174 | 93 | < 0.001 |
| SD | 111.5 | 93.53 | 35.961 | |




**Graph 6 :** Distribution of mean onset of sensory block.

**Table 7:** Distribution of mean onset of motor block.

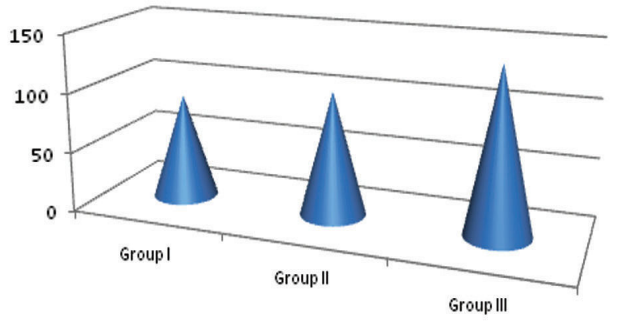
| Onset of motor block | Group I | Group II | Group III | p value |
|---|---|---|---|---|
| No. of Cases | 20 | 20 | 20 | |
| Mean | 155.25 | 109.5 | 57.75 | <0.001 |
| SD | 60.447 | 14.68 | 17.73 | |




**Graph 7:** Distribution of mean onset of motor block.

**Table 8:** Distribution of mean time to two segment regression.

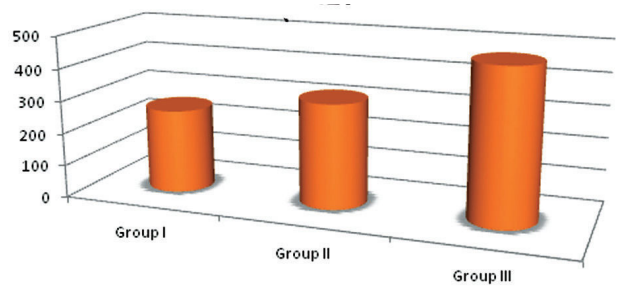
| Two Segment Regression | Group I | Group II | Group III | p value |
|---|---|---|---|---|
| No. of Cases | 20 | 20 | 20 | |
| Mean | 88.5 | 104.25 | 138.75 | <0.001 |
| SD | 14.519 | 17.18 | 27.47 | |




**Graph 8:** Distribution of mean time to two segment regression.

**Table 9:** Distribution of mean time to sensory regression to $L_1$.

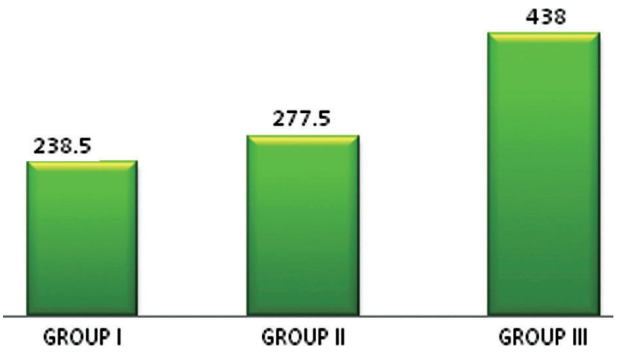
| Time to Sensory Regression to $L_1$ | Group I | Group II | Group III | p value |
|---|---|---|---|---|
| No. of Cases | 20 | 20 | 20 | |
| Mean | 257.25 | 321 | 469.5 | <0.001 |
| SD | 56.39 | 47.03 | 41.03 | |




**Graph 9:** Distribution of mean time to sensory regression to $L_1$.

**Table 10:** Distribution of mean duration of analgesia.

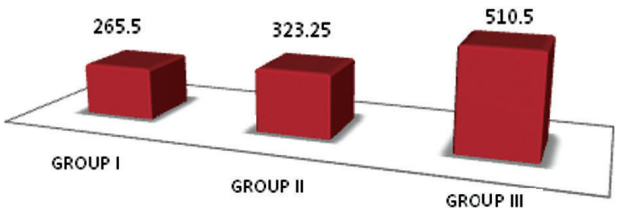
| Duration of Analgesia | Group I | Group II | Group III | p value |
|---|---|---|---|---|
| No. of Cases | 20 | 20 | 20 | |
| Mean | 238.5 | 277.5 | 438 | < 0.001 |
| SD | 81.27 | 75.62 | 97.89 | |




**Graph 10:** Distribution of mean duration of analgesia.

**Table 11**: Distribution of mean duration of motor block.

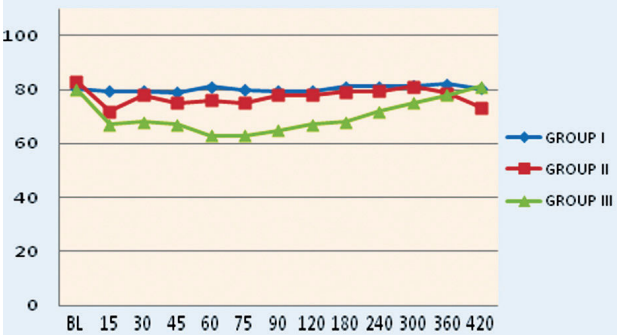
| Duration of Motor Block | Group I | Group II | Group III | p value |
|---|---|---|---|---|
| No. of Cases | 20 | 20 | 20 | <0.001 |
| Mean | 265.5 | 323.25 | 510.5 | |
| SD | 55.72 | 42.83 | 45.18 | |



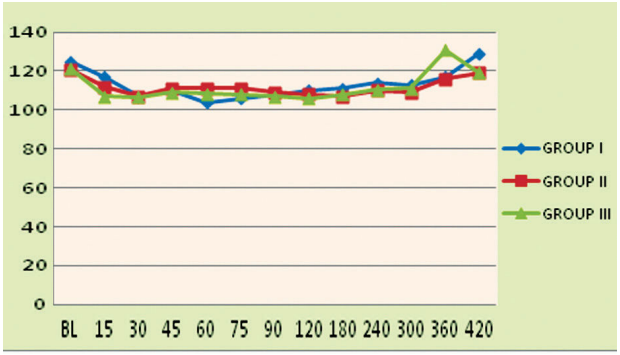

**Graph 11:** Distribution of mean duration of motor block.

**Table 12:** Sedation scores.

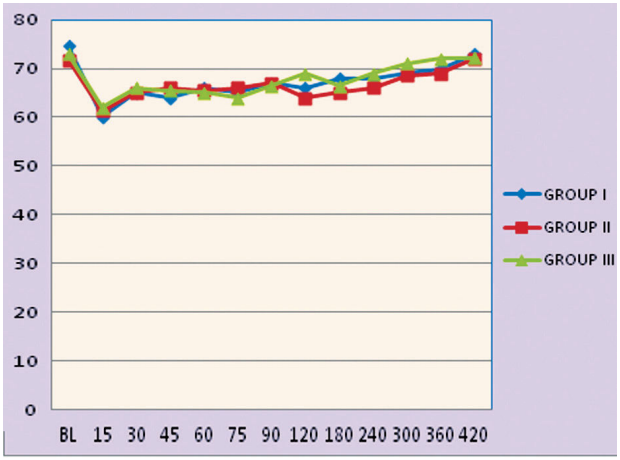
| RSS | Group I | Group II | Group III |
|---|---|---|---|
| 1 | 5 | 0 | 0 |
| 2 | 15 | 20 | 20 |




**Graph 12:** Variation of heart rate among the groups.




**Graph 13:** Variation of mean SBP among the groups.




**Graph 14:** Variation of mean DBP among the groups.

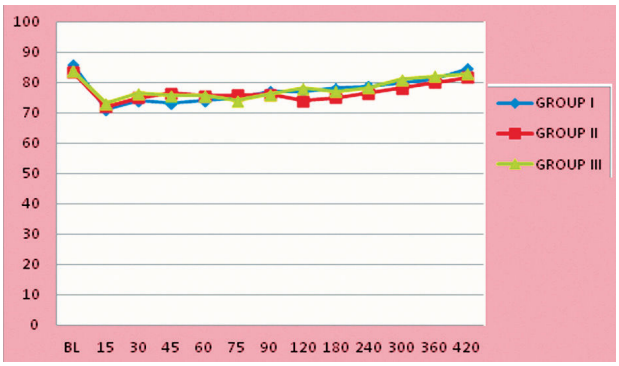
There were statistically significant differences between the three groups with respect to time of onset and regression time of sensory and motor blocks ($p<0.05$). There was rapid onset of sensory (Table 6) and motor blocks (Table 7) in Group III compared to Group II which in turn has a faster onset than Group I. There is significant difference between groups in two segments Regression and mean time to sensory regression to L1 with Group

III requiring a much longer time compared to Group II which is inturn longer than Group I(p<0.001) (Table 8, Table 9).

There is significant difference between groups in total duration of Analgesia with Group III (438min) having a much longer duration compared to Group II (277.5 min) which is longer than Group I (238.5min) (p <0.001)(Table 10).

There is significant difference between groups in duration of motor block with Group III (510.5 min) having longer duration compared to group II(323.25) which is longer than Group I (265.5) (p<0.001)(Table 11).

There is no significant difference between all the 3 groups with respect to intraoperative and postoperative mean heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure with p>0.05 (Graph 12, Graph 13, Graph 14, Graph 15).




**Graph 15:** Variation of MAP by groups.

The median Ramsay sedation score in all the three groups is 2. Therefore, there is no significant difference although 100% of the Dexmedetomidine group cases have a desirable sedation score of 2 (Table 12).

## Discussion

Alpha 2 agonist dexmedetomidine added to local anaesthetics has been shown to provide excellent surgical anaesthesia.

It is thought that intrathecal dexmedetomidine produces its analgesic effect by inhibiting the release of C fibers transmitters and by hyperpolarization of post-synaptic dorsal horn neurons. The prolongation of motor effect might be caused by direct impairment of excitatory amino acid release from spinal interneurons.

The 3 groups are comparable with respect to the patient characteristics and duration of surgery. The mean time to onset of sensory block is statistically significantly faster in group II and III over group I in a dose dependent manner.

It correlates with the study by Al-Mustafa MM et al[6] who found that the mean time of sensory block to reach T10 was 4.7±2 min in D10 group (10 µg dexmedetomidine), 6.3±2.7min in D5 (5µg dexmedetomidine) and 9.5±3 min in group N (control).

Ji Eun Kim, Na Young Kim, Hye Sun Lee[7] also observed that the patients in dexmedetomidine group (D) demonstrated a shorter time to reach the peak sympathetic and sensory block level compared to the patients in control Group,(S) (p<0.01).

The mean time to onset of Bromage 2 motor block shows statistically significant difference among the three groups (p<0.001) in a dose dependent manner.

It correlates with the study by Al-Mustafa MM et al[3] who found that the mean time to reach Bromage 3 scale was 10.4±3.4min with 10 µg Dexmedetomidine,13±3.4 min with 5µg Dexmedetomidine and 18±3.3min in control group.

Kanazi GE et al[10] also found that the patients in who received 12 mg of bupivacaine supplemented with 3 µg of dexmedetomidine intrathecally had faster onset of maximum motor block compared to plain bupivacaine.

In our study, the mean time taken for two segment regression and the time to sensory regression to L1 was significantly prolonged in a dose dependent manner in group II and Group III i.e Group III > Group II > Group I (p < 0.001).

Hala E A Eid MD et al[7] also concluded that Dexmedetomidine significantly prolonged time to two segment regression,sensory regression to S1, in a dose dependent manner.

Al Mustafa MM et al[3] also found that the regression time to S1 dermatome was 338.9±44.8 min in group D10, 277.1±23.2 min in D5 and 165.5±32.9 min in group N (p < 0.001).

There was no statistically significant difference among the groups in maximum level of sensory block, which was T6 level in all the three groups.

It correlates with the study by Hala E A Eid, Mohamed A Shafie, Hend Youssef[7] found that the median and range of the peak sensory level reached were T6 (T3—T10) in group B, T5 (T3—T9) in group D1 and T7 (T4—T9) in group D2, not statistically different among the groups (P=0.08).

Rajni Gupta, Jaishri Bogra, Reetu Verma[6] also found no difference between group D and R in the highest level of block (T5 and T6, respectively)

when dexmedetomidine was added to ropivacaine as intrathecal adjuvant (D) vs Control (R).

There is significant difference between groups in total duration of analgesia with Group III (438 min) having a much longer duration compared to Group II (277.5 min) which is longer than Group I (238.5 min) ($p < 0.001$). Thus, the analgesic requirement in the first 24 hours postoperatively in Group III was significantly lesser than that in Group II which was inturn lesser compared to that in Group I.

Hala E A Eid, Mohamed A Shafie, Hend Youssef[7] concluded that intrathecal dexmedetomidine in doses of 10 µg and 15 µg significantly increased the duration of analgesia provided by spinal bupivacaine by about 240 or 520 min respectively. The increased duration of analgesia in their study may be due to the lower dermatomal levels needed in anterior cruciate ligament surgery for pain relief in comparison to our study which included abdominal surgeries as well which require higher dermatomal levels of sensory blockade.

The median of the maximum motor block attained is Bromage Grade 4 in all the 3 groups. Therefore, there is no statistical difference between the groups in this regard.

Hala E A Eid, Mohamed A Shafie, Hend Youssef[7] found that all the patients achieved modified Bromage 3 motor block.

Ji Eun Kim, Na Young Kim ,Hye Sun Lee[8] also observed that the peak block level was similar for the two groups receiving either dexmedetomidine 3 µg (n=27) or normal saline (n=27) intrathecally with 6 mg of 0.5% hyperbaric bupivacaine.

The mean duration of motor block in Group I,II and III shows statistically significant difference, with a dose related prolongation of the duration of motor block.

It correlates with the study by Hala E A Eid, Mohamed A Shafie, Hend Youssef[7] who found that motor block regression to modified Bromage 0 were significantly prolonged in group D2 (15µg dexmedetomidine) than in group D1 (10µg dexmedetomidine) and group B (control) and in group D1 than in group B.

Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS et al[3] observed that the regression to Bromage 0 was 302.9±36.7min in D10 (10µg dexmedetomidine), 246.4±25.7min in D5 (5µg dexmedetomidine) and 140.1±32.3 min in group N (control). Onset and regression of motor block was highly significant (N versus D5, N versus D10 and D5 versus D10, $p<0.001$).

In our study,there is no significant difference between all the 3 groups with respect to intraoperative and postoperative mean heart rates, mean SBP, DBP and MAP with $p>0.05$. Thus, the haemodynamic stability is maintained even in the presence of Dexmedetomidine.

It correlates with the study by Hala E A Eid, Mohamed A Shafie, Hend Youssef[7] who found that the mean values of MBP and HR were comparable between the three groups throughout the study duration.

Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS et al[3] also observed that the three groups in their study had comparable haemodynamics throughout the period of study.

The median Ramsay sedation score in all the three groups is 2. Therefore, there is no significant difference although 100% of the cases in the Dexmedetomidine groups (II and III) have a desirable sedation score of 2.

Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS et al[3] also observed that all the patients in the three groups in their study had a RSS of 2. Hala E A Eid, Mohamed A Shafie, Hend Youssef[7] found that the patients in group B and group D1 had a median RSS of 2 (2-3) at all assessment times ($P> 0.05$). Patients in Group D2 had a higher median sedation score (3.5 -4) between 60 mins and 195 mins ($p < 0.05$).There was no significant difference in the sedation scores between the groups at the other time points.

The incidence of hypotension and thus use of vasopressor was higher in group II and III (30%) than in group I (15%). The incidence of bradycardia and thus use of atropine was higher in group II and III (30% and 35% respectively) than in group I (25%). These differences were found to be statistically insignificant. 25% of the patients in group I were anxious whereas all the patients of the dexmedetomidine groups (II and III) were tranquil. All the patients had a peripheral oxygen saturation greater than 95% at all times and did not require additional oxygen.

No patient had respiratory rate below 10/ min. Two patients in group I and one in group III had shivering,which was managed with i.v Tramadol 25 mg. No patient reported pruritus. Complete recovery of sensory and motor function was observed in all studied patients.Two weeks after surgery at the postoperative follow up visit, patients did not show any neurological deficit.

## Conclusion

I conclude that 15µg of dexmedetomidine added to local anaesthetic in subarachnoid block has proved to be a better adjuvant in prolonging the sensory and motor blockade intraoperatively and the duration of postoperative analgesia compared to 10µg ,without significant adverse effects. It is an attractive option for prolonged surgeries of the lower limb precluding the need for use of general anaesthetics and epidural anaesthesia.

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