



## Original Research Article

## A comparison of intrathecal low dose Dexmedetomidine and clonidine as an adjuvant to bupivacaine in patients undergoing gynecological surgeries

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## ABSTRACT

**Introduction:** In the anquity of post-operative analgesia, the inception of  $\alpha$ -2 adrenergic agonist agents in subarachnoid space with adjuvance to bupivacaine has opened new chapter.

**Aims:** The intent of the study was to compare the onset of duration of sensory and motor block, hemodynamic effects, post-operative analgesia and adverse effects of dexmedetomidine and clonidine with hyperbaric 0.5% bupivacaine for spinal anaesthesia.

**Materials and Methods:** Sixty adult patients received subarachnoid block either with Injection Bupivacaine (15mg) with clonidine (30 $\mu$ g) or Injection Bupivacaine (15mg) with Dex medetomidine (10 $\mu$ g). Patients were monitored for variations in heart rate and noninvasive blood pressure after the spinal anaesthesia was given till the surgery got over every 5 minutes. Both the groups were compared for onset time for sensory block, time to reach sensory block to T<sub>10</sub> and T<sub>6</sub> level, time of regression of sensory block by 2 dermatomes and duration of analgesia.

**Results:** Mean Onset time of sensory block, time to reach T<sub>10</sub> and T<sub>6</sub> level was greater but not significant in Dexmedetomidine group but regression time of sensory block by 2 dermatomes was significantly higher in clonidine group, 100.21 $\pm$ 2.58 minutes as compared to 80.43 $\pm$ 3.45 in dexmedetomidine group. Onset time to reach bromage II was significantly faster in group BD (35.53  $\pm$  3.57seconds) as compared to Clonidine group (49.03  $\pm$  30.15seconds). Dexmedetomidine group patients had significantly (p<0.0001) higher duration of analgesia (589  $\pm$  5.5minutes) as compared to Group clonidine (507  $\pm$  4.8minutes). There was no sedation and no hemodynamic instability observed in either of the groups.

**Conclusions:** We conclude that though both Clonidine and Dexmedetomidine prolongs duration of sensory and motor block of Bupivacaine, But Dexmedetomidine is more appropriate as it provides better VAS score (quality) and longer duration of postoperative analgesia than clonidine.

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### 1. Introduction

Postoperative diminution of pain is the sole essence of Anaesthesia. Ever since the introduction of local anaesthetics, Anaesthesiologists and physicians investigated different modes of using them. Spinal Anaesthesia has emerged as one of the important technique which is simple effective and safe with history since its introduction. Any drug when added to local anaesthetic agent intrathecally, forms reliable and reproducible method of postoperative analgesia. In the past various drugs has been used

and opioids are among them which ineluctably does not cause motor or autonomic blockade.<sup>1,2</sup> But presence of side effects like nausea vomiting, respiratory depression urinary retention incited further research towards non-opioid analgesics who are devoid of these side effects.

Many studies have undergone to improve the quality of subarachnoid block and found that  $\alpha$ <sub>2</sub> Adrenergic agonists are new such neuraxial adjuvants. Clonidine, an  $\alpha$ <sub>2</sub> Adrenergic receptor agonist has 200 : 1 times affinity ratio of  $\alpha$ <sub>2</sub>:  $\alpha$ <sub>1</sub> receptors while Dexmedetomidine who is selective  $\alpha$ <sub>2</sub> Ad renergic receptor agonist has 620 : 1 respectively. Dexmedetomidine also displays protective and growth promoting properties in tissues which includes nerve

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cells from cortex. It has neuroprotective effect similar to methylprednisolone when given in spinal cord injury.<sup>3,4</sup>

We compared the collegial effect of clonidine and Dexmedetomidine to hyperbaric bupivacaine when given intrathecally analogous to onset and duration of sensory and motor blockade analgesia and quality of VAS Score.

## 2. Materials and Methods

After obtaining approval from the Institutional ethical committee, a prospective randomized single blinded study was conducted in 60 patients of 18-65 yrs of ASA (American society of Anaesthesiologists) physical status I and II who were posted for elective Gynaecological surgeries (Table 2) in our Hospital from July 2019 to November 2019.

Patients belonging to ASA physical Status III and IV or patients having significant cardiovascular, renal or hepatic dysfunction, morbidly obese patients, or patients having allergy to drugs used or contraindication to subarachnoid block were excluded from the study.

Computer generated randomization was used to allocate the patients into 2 groups. Each comprising of 30 patients.

Group BC: Patients received Injection Bupivacaine 15mg with 30  $\mu$ g clonidine

Group BD: Patients received Injection Bupivacaine 15mg with 10  $\mu$ g dexmedetomidine

Informed consent from the patients were taken and then they were enlisted in the study. Patients were explained about Visual Analogue Scale score (VAS) in preoperative visit and again was repeated in the operating room. Patients were given tablet Ranitidine Hydrochloride 150 mg in the night previous to the surgery day. Patients were fasted overnight. Routine investigations which was advised in for preoperative visit was checked on the operative day.

In the operating room patients were preloaded with Ringer lactate 15ml/kg IV after securing the intravenous line with Intravenous cannula of 18 or 20 gauge. Monitors were applied and baseline vitals like Heart Rate (HR), Respiratory Rate (RR), ECG, O<sub>2</sub> saturation (SpO<sub>2</sub>) and noninvasive Blood pressure (BP) were recorded. Subarachnoid block was given with spinal needle in L 2-3 space in sitting position using aseptic precautions and drug was injected in subarachnoid space after confirming the free flow and clear aspiration of CSF (cerebro - spinal fluid). Patients were made supine and following parameters were noted.

1. Time of onset and achieving T<sub>10</sub> of sensory blockade
2. Onset Time of motor blockade
3. Time required to achieve Maximum sensory blockade
4. Sensory regression time by two segments
5. Intraoperative sedation scoring
6. Time when first rescue analgesia was given (total duration of analgesia)

7. Any adverse events like hypotension, bradycardia, pruritis, nausea vomiting or respiratory depression if occurred
8. Vital parameters

In our study appearance of tingling sensation in the limbs was taken to be onset of sensory analgesia and time to achieve T<sub>10</sub> and highest segmental level reached was checked by pin prick method. Onset of motor block was determined by inability to raise extended limb but able to move legs and feet (stage II of modified Bromage criteria) was noted. Total duration of analgesia was defined as the time duration from the giving of spinal anaesthesia to first request of rescue analgesia (injection Diclofenac Sodium 75 mg IV). Quality of analgesia was assessed by VAS. Motor blockade was assessed using modified Bromage scale. Sedation was assessed by Ramsay sedation scale and hemodynamic parameters (HR, mean arterial pressure (MAP), and SPO<sub>2</sub>) were recorded at 2 min interval up till 10 minutes and there after every 5 minutes till the surgery got over. Any adverse events like hypotension, bradycardia, nausea pruritis and respiratory depression were also recorded. Hypotension was defined when the blood pressure decreased  $\geq 30\%$  of the base line ; brady cardia was defined as decrease in heart rate  $\geq 20\%$  of the base line values.

### 2.1. Statistical analysis

Sample size was taken as 60. Data analysis was performed by using Statistical Package SPSS by Microsoft excel 2010. Data were expressed as mean  $\pm$  standard deviation. Chi square test was used to identify the distribution of variables and continuous variables were analyzed by ANNOVA. Statistical significance was determined by subject t-test. Two tailed p values were used throughout and p value  $< 0.05$  was taken as statistical significant with 1- $\beta$  80% sensitivity.

## 3. Results

There was no analytical variance in patients' demographic datas, duration and type of surgery or ASA physical status as shown in Tables 1 and 2.

In our study we marked appearance of tingling sensation as onset of sensory blockade which was  $10.76 \pm 1.47$  seconds in Group BC and  $12.28 \pm 6.97$  seconds in Group BD. the disparity in both the groups was not significant with p value = 0.116. Table 3.

Time to reach T<sub>10</sub> dermatome  $81.86 \pm 7.74$  seconds and  $80.16 \pm 43.21$  seconds in group BC and BD respectively, difference again was analytically not significant (p=0.832) Table 3.

Time to reach T<sub>6</sub> dermatome was  $87.86 \pm 7.74$  seconds in group BC and  $86.03 \pm 43.21$  seconds in group BD with p=0.8202 suggesting insignificance. Table 3

Mean time of sensory regression by 2 segments was  $100.21 \pm 2.58$  minutes in group BC whereas it was  $80.43 \pm 3.45$  minutes in group BD which was highly significant  $p < 0.0001$  Table 3.

Mean time of onset of motor block (Modified bromage scale II) was  $49.03 \pm 30.15$  seconds in group BC whereas it was  $35.53 \pm 3.57$  seconds in group BD which was significant  $p = 0.0180$  Table 3.

Mean Time for rescue analgesia was  $507 \pm 4.8$  minutes in group BC and  $589 \pm 5.5$  minutes in group BD. (highly significant) Table 3.

Maximum dermatome achieved: 16.66% patients achieved T4 dermatome and 83.33% achieved T6 level in group BC whereas 40% patients achieved T4 dermatome level and 60% patients achieved T6 dermatome in group BD. Table 4

Mean VAS Scores postoperatively at 2 hr was 0.166 in group BC and  $0.36 \pm 0.49$  in group BD which was significant and remained significant up till 6th hour postoperatively where mean VAS score was  $2.8 \pm 0.71$  in group BC and was  $2.83 \pm 0.37$  which was not significant with p value 0.8381 and thereafter it was significant again up till 11<sup>th</sup> hour as shown in Table 5. Mean VAS score at all times was  $2.725 \pm 1.3$  in group BC and  $2.41 \pm 1.8$  in group BD which was highly significant  $p < 0.0001$ .

Adverse Events: 16.66% patients of group BC had bradycardia while only 10% patients experienced bradycardia in group BD. 20% patients in group BC had hypotension while only 6% in group BD. but 2 patients in group BC and one patient in group in BD patient was treated with single injection of mephentermine 6 mg IV and none of either group of patient required treatment for bradycardia. (Figure 1)

Mean heart rate was comparable in both the groups. Though the difference in the mean arterial blood pressure was significant after 30 minutes but the fall of Mean arterial blood pressure in individual group from baseline was not significant.

#### 4. Discussion

One of the major goals of Anaesthesia is quelling of pain. With the technical skill and pharmacological knowledge anaesthesiologists are in paradigmatic position to treat pain during intraoperative and postoperative period and intent of good postoperative analgesia is to produce perennial, perdurable, continuous effective analgesia with minimal side effects. Hence an intrathecal additive to local anaesthetics forms dependable and predictable method to perpetuate the duration of anaesthesia with protracted post operative analgesia. Spinal Anaesthesia technique being simple and convenient has gained a wide recognition.

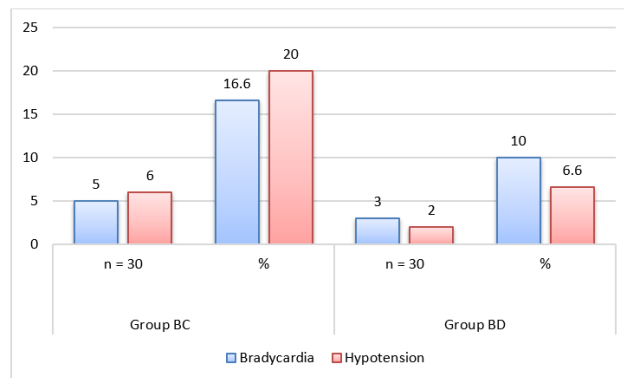


Fig. 1:

Dexmedetomidine and clonidine both are  $\alpha_2$  adrenoceptor agonists drugs which were initially used for treating hypertension and giving sedation and perceptibly the role of these two drugs unfurled in operation theatre for intraoperative and postoperative analgesia and sedation.

Al –Mustafa MM<sup>5</sup> et al and Shagufta Naaz<sup>6</sup> et al studied for the optimum dose of Dexmedetomidine and came to conclusion that there was significant prolongation of analgesia with nominal side effects when author used  $10 \mu\text{g}$  dexmedetomidine intrathecally as an adjuvant to hyperbaric Bupivacaine.

Kanazi<sup>7</sup> et al found that there were minimal side effects and maximal prolongation of analgesia when clonidine was used in dose of  $30 \mu\text{g}$  as an adjuvant to hyperbaric bupivacaine. So on the basis of these studies we adopted  $10 \mu\text{g}$  Dexmedetomidine and  $30 \mu\text{g}$  of clonidine and evaluated their analgesic efficacy as adjuvants to  $15 \text{mg}$  hyperbaric bupivacaine when given intrathecally in patients posted for gynecological surgeries in our hospital.

The function of local anaesthetic is to block the sodium channels whereas  $\alpha_2$  adrenoceptor agonists by binding to presynaptic C- fibers and post synaptic dorsal neurons depresses its release by hyperpolarisation of post synaptic dorsal horn neurons.<sup>8–12</sup> This explains how they prolong sensory block when combined to spinal anaesthetics.

In our study Group BC had earlier onset of sensory block at T<sub>10</sub> and T<sub>6</sub> dermatome than group BD and this was comparable to the studies conducted by Kanazi<sup>7</sup> et al, Saxena<sup>13</sup> et al and Shukla<sup>14</sup> et al.

The maximum sensory level achieved in group BC (16.66%) and group BD (40%) was T<sub>4</sub> which was in conconanc e with the studies conducted by Kanazi<sup>7</sup> et al, Strebil<sup>15</sup> et al and Gupta<sup>16</sup> et al.

$\alpha_2$  adrenoceptor agonists binds to motor neurons in the dorsal horns and thus resulting in the prolongation of motor block.<sup>17</sup> In our study mean onset time of motor blockade was earlier in group BD which was significant and was in agreement with the study conducted by Saxena<sup>13</sup> et al, Shukla<sup>14</sup> et al and Grande<sup>17</sup> et al.

**Table 1:** Demographic profile

Mean $\pm$ SD	Group BC	Group BD	p value
Age (yrs)	31.64 $\pm$ 9.12	30.82 $\pm$ 8.4	0.716
ASA I:II	20:10	21:9	
BMI kg/m <sup>2</sup>	24.21 $\pm$ 2.21	23.24 $\pm$ 2.26	0.09
Duration of surgery (min)	87.33 $\pm$ 13.56	79.83 $\pm$ 19.58	0.08

**Table 2:** Type of surgeries

	Group BC	Group BD
AH	5	6
VH	6	7
Myomectomy	2	5
Salpingo-Oophorectomy	1	2
ovaian mass	2	3
VH + TOT	4	1
VH + AP repair	3	2
p sling	3	2
AH + salpingo-oophorectomy	4	1
Cystocele repair	0	1
Total	30	30

**Table 3:** Characteristics of spinal block

Mean $\pm$ SD	Group BC	Group BD	p value
Sensory onset Seconds	10.76 $\pm$ 1.47	12.83 $\pm$ 6.97	0.1169
Time to reach T10 dermatome (seconds)	81.86 $\pm$ 7.74	80.16 $\pm$ 43.21	0.8328
Time to reach T6 dermatome (seconds)	87.86 $\pm$ 7.74	86.03 $\pm$ 43.21	0.8202
Time for 2 segment regression(minutes)	100.21 $\pm$ 2.58	80.43 $\pm$ 3.45	<0.0001
Motor onset (seconds)	49.03 $\pm$ 30.15	35.53 $\pm$ 3.57	0.0180
Time for rescue analgesia (minutes)	507 $\pm$ 4.8	589 $\pm$ 5.5	<0.0001

**Table 4:** Maximum dermatome achieved

	Group BC n=30	%	Group BD n=30	%
T4	5	16.66	12	40
T6	25	83.33	18	60

**Table 5:** Mean VAS scores Postoperatively

Mean $\pm$ SD Postoperatively	Group BC	Group BD	p value
1st Hour	0	0	
2nd hour	0.166 $\pm$ .37	0.36 $\pm$ 0.49	<0.0001
3rd hour	1.13 $\pm$ 0.43	1 $\pm$ 0.10	=0.1122
4th hour	2.03 $\pm$ 0.55	1.4 $\pm$ 0.50	<0.0001
5th hour	2.73 $\pm$ 0.73	2 $\pm$ 0.10	<0.0001
6th hour	2.8 $\pm$ 0.71	2.83 $\pm$ 0.37	=0.8381
7th hour	3.76 $\pm$ 0.73	3.46 $\pm$ 0.50	=0.0684
8th hour	4.44 $\pm$ 0.65	3.9 $\pm$ 0.48	=0.0005
9th hour	4.75 $\pm$ 0.45	4.4 $\pm$ 0.50	=0.0060
10th hour		4.68 $\pm$ 0.40	
11th hour		5.0	

Time taken for regression of sensory blockade by 2 segments was earlier in group BD and was significantly more in group BC.

Both Dexmedetomidine and clonidine produces analgesia by activating  $\alpha_2$  adrenoceptors in the spinal cord by reducing transmission of adrenoceptors nociceptive signals. Kalso<sup>18</sup> et al appealed that Dexmedetomidine has 10 times more affinity to  $\alpha_2$  receptor than clonidine which can be seen in our study where group BD produces significantly longer duration of analgesia which is also in agreement with the study conducted by Grande<sup>17</sup> et al, Gupta<sup>16</sup> et al, Chabra<sup>19</sup> et al and Abdel Hamid<sup>20</sup> et al.

Mean VAS scores were significantly lower at all times in the group BD than group BC suggesting better quality of post operative analgesia in group BD. Our study findings were comparable to the study done by Abdelhamid<sup>20</sup> et al and Ashar Amin<sup>21</sup> et al.

$\alpha_2$  Agonists stimulate  $\alpha_2$  receptors in the brain and spinal cord and inhibits neuronal firing which leads to hypotension and bradycardia. All patients in our study were preloaded with ringer lactate injection 15ml/kg, this could be the reason that despite the fall in blood pressure, Hypotension and Bradycardia was not appreciated in both the groups. It could be also be due to the dose selection of both the drugs (with minimal side effects).

The sedation effect of  $\alpha_2$  agonists is postulated to be in the locus coruleus in the brainstem which is also origination site for descending medullospinal adrenergic pathways, key mechanisms in regulating nociceptive neurotransmission. Sedation was assessed using Ramsay sedation score at regular intervals and it was comparable in both the groups. All of the patients were in stage II, Patient were cooperative, oriented, and tranquil alert and none were anxious, agitated, or restless.

## 5. Conclusion

We conclude that though both Clonidine and Dexmedetomidine prolongs duration of sensory and motor block of Bupivacaine, But Dexmedetomidine is a better choice in terms quality and longer duration of postoperative analgesia.

## 6. Source of funding

None.

## 7. Conflict of interest

None.

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