Original Research Paper

Volume-9 | Issue-2 | February-2019 | PRINT ISSN - 2249-555X

Anaesthesioilogy

EFFECTS OF INTRAVENOUS DEXMEDITOMIDINE ON HYPERBARIC BUPIVACAINE SPINAL ANAESTHESIA A RANDOMIZED CONTROL STUDY

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KEYWORDS :

INTRODUCTION

Spinal anaesthesia with local anaesthetic agents is extensively used for lower abdominal surgeries. The pain relief yielded by spinal anaesthesia is excellent compared to intravenous or epidural anaesthesia.There are many advantages of spinal anaesthesia over general anaesthesia which makes it the anaesthesia of choice in current surgical practice. Since it decreases the duration of stay, it is cost effective for both patient and hospital. It is suitable for patients with respiratory diseases and helps in preventing intubation related problems like laryngospasm. It is also helpful in maintaining the airway patency and reduces blood loss[2].

One of the main disadvantages is the limited duration of block achieved with local anaesthetics. To overcome this, various adjuvants have been tried and used successfully.

This addition of adjuvant has further expanded the advantage of regional anaesthesialike rapid onset of action, reduces the local anaesthetic requirements, reduces the risk of local anaesthetic toxicity, prolongs the sensory block,improves the analgesic quality, improves the hemodynamic stability, improved and prolonged duration of postoperative analgesia.

α2-agonists like clonidine and dexmedetomidine havebeen used to prolong spinal anesthesia. Apart from sedation and analgesia, they also decrease the sympathetic tone and the stress responses to surgery and anesthesia. Dexmedetomidine is a more selective α2-A receptor agonist compared to clonidine, with higher sedative and analgesic effects. Few studies have shown the efficacy of intravenous (IV) dexmedetomidine in prolonging spinal anesthesia in addition to providing good sedation and postoperative analgesia.

This research is designed to study the efficacy of such combination in our institution and compare the results with the previous studies done at other institutions.

AIM OF THE STUDY

The present study is designed to evaluate

1. Onset of sensory and motor blockade
2. Duration of sensory and motor blockade
3. Hemodynamic effects of intravenous dexmedetomidine on spinal anesthesia.
4. Sedation levels
5. Adverse effects

MATERIALS AND METHODS

This study was carried out in the gynaecology theatre, Raja Mirasudar Hospital, attached to Thanjavur Medical College Hospital, Thanjavur.

A Prospective double blinded randomized control study was conducted on 60 ASA I and ASA II patients undergoing total abdominal hysterectomy under spinal anaesthesia who fulfill the inclusion criteria

The study was started after receiving institutional ethical committee approval and patients were randomly divided in to two groups namely Group BD and Group BB. Before including the patients for the study, all patients were explained about the procedures and a written informed consent was obtained.

INCLUSION CRITERIA:

1. American society of Anaesthesiologists (ASA) grade I-II
2. Age 30-60 years

EXCLUSION CRITERIA:

1. Hb < 8g/dl or
2. Patients receiving calcium channel blockers , ACE inhibitors, clonidine & Beta blockers.
3. Patients on sedative medications, opioids and antidepressants prior to surgery.

PREOPERATIVE PREPARATION:

After routine preoperative assessment, patients base line mean arterial pressure, pulse rate, oxygen saturation were recorded. Intravenous line started. The patients were randomly allocated into two groups of 30 each by using closed cover technique.

In the operating room, appropriate equipment for airway management and emergency drugs were kept ready. The horizontal position of the operating table was checked. Patients were shifted to the operating room and positioned.

Non-invasive blood pressure monitor, pulse oximeter and ECG leads were connected to the patient. Preoperative baseline systolic and diastolic blood pressure, mean arterial pressure, pulse rate and oxygen saturation were recorded. Patients were preloaded with 10ml/kg of ringer lactate 15minutes prior to the subarachnoid block. On right lateral position, the skin over the back was prepared with antiseptic solution and draped with sterile towel.

After skin infiltration with 2% lidocaine , 25G Quincke's needle was inserted at the L3/4 interspace in the midline. After confirming free flow of CSF, subarachnoid block was performed with 3.5ml of 0.5% bupivacaine in both groups. The patients were made to lie supine immediately after injection and the time at which the spinal anaesthesia performed was noted

GROUP BD:

Immediately following subarachnoid block patients received a loading dose of 1microgram/kg dexmedetomidine IV by infusion pump over 10min followed by maintanence dose of 0.5microgram/kg/hr till the end of surgery.

GROUP BB:

Immediately following subarachnoid block patients received an equivalent quantity of normal saline as group BD as loading and maintanence dose by IV infusion pump.

The following parameters were noted 1,Time of injection of subarachnoid block. 2,Time of onset of sensory block at T10 level.3, Time of onset of motor block. 4,Two dermatomal regression time 5,Duration of sensory block. 6,Duration of motor block.7,Degree of sedation and 8,Adverse effects.

Systolic and Diastolic blood pressure, Mean Arterial Blood pressure, pulse rate and oxygen saturation were recorded at 0 , 5th minute and thereafter every 5 minutes upto 30 minutes and then every 10 minutes till the end of the procedure.

Hypotension was said to have occurred if the MAP fell less than 60 mmHg and was treated with supplemental O2, increasing the infusion rate of IV fluids and Inj. Ephedrine in incremental doses of 6mg at interval of 2 minutes.

Bradycardia was defined as heart rate less than 60/min and was managed with intravenous atropine in incremental doses.

Any discomfort like nausea, vomiting, shivering, pruritus and adverse events such as hypotension, bradycardia, respiratory depression and ECG changes were noted .Vomiting was managed with Inj.Ondansetron 4mg intravenously.

On completion of surgery, patient was shifted to post anaesthesia care unit for observation. Patients were transferred to postoperative ward after complete resolution of motor blockade and stabilization of blood pressure. Vital signs and oxygen saturation were recorded til recovery of patients from anaesthesia. Injection Diclofenac sodium 75mg was given intramuscularly when the patient complained of pain in the postoperative period (rescue analgesic).

SENSORY BLOCK:
The **onset** of sensory block was defined as the time between the injection ofanaesthetic solution and the absence of pain at the T10 dermatome. Sensory blockwas assessed by loss of sensation to pin prick using 25G sterile needle bilaterally along the midclavicular line. This assessment started immediately after turning the patient to supine position and continued every minute till loss of sensation to pinprick at T8 level was noted. The **duration** of sensory block was defined as the time between the intrathecal administration of anaesthetic solution and the first supplementation of rescue analgesic when patient complained of pain.

MOTOR BLOCK :
Motor block was assessed bilaterally using Bromage scale.

BROMAGE SCALE
0- No block.Able to raise extended legs against gravity.
1- Unable to raise extended legs, but just able to flex knees.
2- Unable to flex knees but able to flex ankles.
3- Total block. Inability to flex ankle/ move leg.

Assessment of motor block was started immediately after turning the patient to supine position and continued every minute till Bromage score of 3 was reached.

The **onset** of motor block was defined as the time to achieve Bromage score of 3 from the time of intrathecal injection. **Duration** of motor block was taken as the time from intrathecal injection to return of Bromage score of 0 (complete recovery).

SEDATION:
RAMSAY SEDATION SCORE was used to assess the degree of sedation.
1. Anxious and Agitated.
2. Cooperative, oriented, tranquil
3. Responds only to verbal commands
4. Asleep with brisk response to light stimulation
5. Asleep with sluggish response to light stimulation
6. Asleep without response to light stimulation

DURATION OF ANALGESIA :
The duration of analgesia was defined as the time between the injection of the drug in to the intrathecal space and the first occasion when patient complaints of pain.

OBSERVATION ANDRESULTS
1. AGE DISTRIBUTION
The age distribution in Group BB and Group BD was comparable. The difference was not significant (p value = 0.67) (table.1).

2. ONSET OF SENSORY BLOCK
Table .1, Time of onset of sensory block among the two groups

Time of onset of sensory block in (minutes)	Range	Mean	SD	P value
Group BB	1-3	2.27	0.64	0.00
Group BD	1-2	1.27	0.45	

The time of onset of sensory block was faster in Group BD (1.27± 0.45) when compared to Group BB (2.27± 0.64) and the difference was significant (p = 0.00) (Table.2, Fig.1).

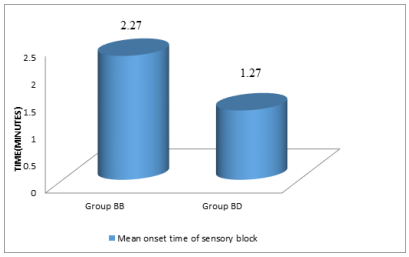

Fig1. Mean onset time of sensory block

3,ONSET OF MOTOR BLOCK
Table .2, Time of onset of motor block among the two groups

Time of onset of motor block (minutes)	Range	Mean	SD	P value
Group BB	3-5	3.37	0.72	0.00
Group BD	2-5	2.28	0.49	

The average time taken for the onset of motor block was 3.37 minutes in Group BB and 2.28 minutes in Group BD. The difference was significant (p = 0.00) (Table.3, Fig.2).

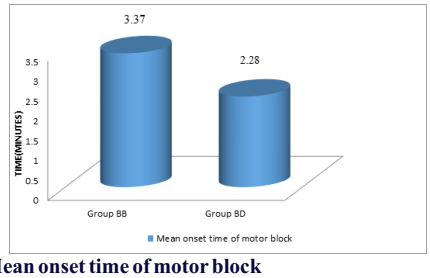

Fig 2. Mean onset time of motor block

3 ,DURATION OF SENSORY BLOCK
Table .3, Duration of sensory block among the two groups

Duration of sensory block in (minutes)	Range	Mean	SD	P value
Group BB	170-280	218.00	31.56	0.00
Group BD	270-500	337.33	73.76	

The mean duration of sensory block was longer in Group BD(337.33 ± 73.76) when compared with Group BB (218 ± 31.56). The difference was significant (p value= 0.00) (Table.4, Fig.3).

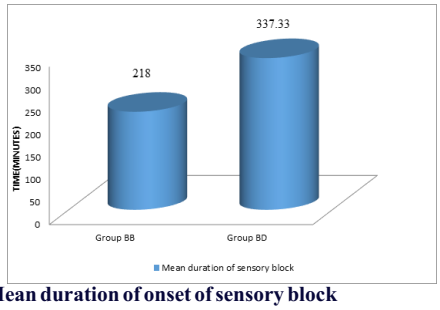

Fig 3. Mean duration of onset of sensory block

The mean duration of sensory block was longer in Group BD(337.33 ± 73.76) when compared with Group BB (218 ± 31.56). The difference was significant (p value= 0.00) (Table.4, Fig.3).

3. DURATION OF MOTOR BLOCK
Table .4, Duration of motor block among the two groups

Duration of motor block (minutes)	Range	Mean	SD	P value
Group BB	140-220	167.67	19.77	0.00
Group BD	210-360	248.33	37.24	

The mean duration of motor block was longer in Group BD (248.33 ± 37.24) when compared with Group BB (167.67 ± 19.77). The difference was significant (p value = 0.00) (Table.5, Fig.4).

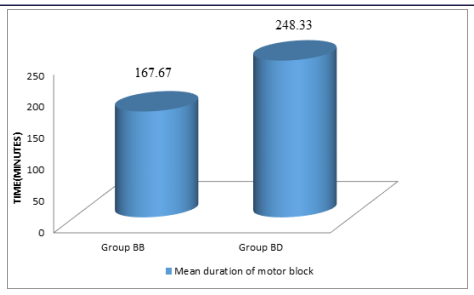

Fig 4. Mean duration of motor block

4. DURATION OF TWO DERMATOMAL REGRESSION

Table .5, Duration of two dermatomal regression among the two groups

Duration of two segment regression (minutes)	Range	Mean	SD	P value
Group BB	90-150	113.67	16.50	0.00
Group BD	100-180	143.87	22.01	

The time taken for two dermatomal regression was longer in Group BD (143.87 ± 22.01) when compared with Group BB(113.67 ± 16.50). The difference was significant (p value = 0.00) (Table.6, Fig.5).

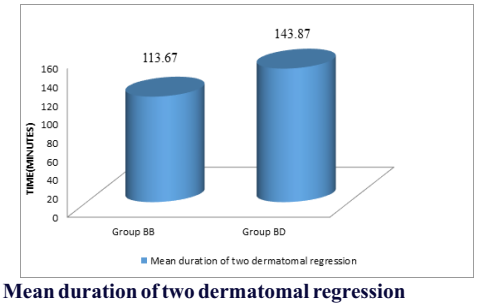

Fig 5. Mean duration of two dermatomal regression

5. DEGREE OF SEDATION

Table .6, Degree of sedation among the two groups

Degree of sedation	Range	Mean	SD	P value
Group BB	1.75-3	2.033	0.215	0.00
Group BD	3-4	3.267	0.321	

The degree of sedation as assessed by Ramsay sedation scale was higher in Group BD (3.267± 0.321) when compared with Group BB (2.033±0.215). The difference was significant (p value = 0.00) (Table.7, Fig.6).

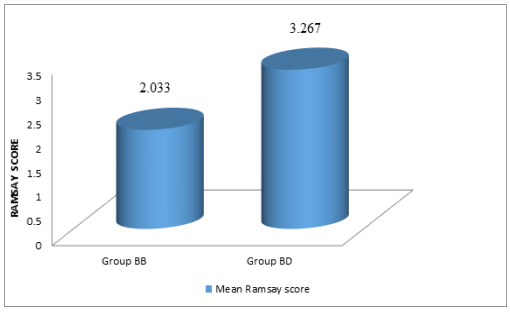

Fig 6 , Mean Ramsay score

6. HEMODYNAMIC VARIABLES

6.1 MEAN ARTERIAL PRESSURE

The mean arterial pressure was monitored from preoperative basal to 60th minute of the procedure. None of the intervals had significant difference in MAP between the two groups .

PULSE RATE

The pulse rate was monitored from preoperative basal to 60th minute of the procedure. There was significant difference in the pulse rate between the two groups from 15minutes to 60 minutes. Group BD had lower pulse rate than Group BB and the difference was significant (Table.9, Fig.8).

Table .7, Mean pulse rate among the two groups

Time interval (minutes)	Group BB Mean ± SD Deviation	Group BD Mean ± SD Deviation	P value
0	97.83±12.823	98.07±16.222	0.95
5	89.23±16.164	87.77±16.132	0.73
10	86.20±14.192	78.43±17.923	0.07
15	84.53±12.969	74.57±17.809	0.02
20	81.73±12.259	72.70±15.572	0.02
25	82.73±11.014	72.00±13.537	0.00
30	81.40±11.907	70.50±11.936	0.00
40	81.73±10.511	73.30±12.166	0.01
60	83.13±11.079	76.50±11.141	0.02

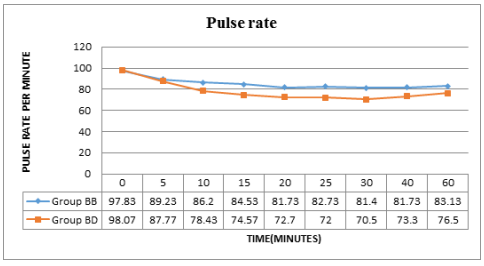

Fig.7. Mean pulse rate among the two groups

6.2 SATURATION

Oxygen saturation was in the range of 97 – 100 % in both groups. The difference in the mean SpO2 was not significant (p value 0.97) (table.10).

ADVERSE EFFECTS

None of the patients in group BB developed bradycardia while 7 patients (23.33%) in Group BD developed bradycardia and received atropine. The difference was significant (p= 0.01).

In Group BB, 4 patients (13.33%) had hypotension while 5 patients (16.67%) in Group BD had hypotension and received ephedrine. The difference between the two groups was not significant (p= 0.76).

None of the patients in Group BD had post-op shivering while 6 patients in Group BB had post-op shivering. The difference between the two groups was significant (p= 0.02).

Five patients (16.67%) in group BB and 4 patients (13.33%) in group BD had vomiting in the post-operative period but the difference between the groups was not significant (Table.11),

DISCUSSION

Subarachnoid block with bupivacaine has been most extensively used for lower abdominal surgeries because of its simplicity, speed, reliability and minimal exposure to depressant drugs. However, a single intrathecal injection of bupivacaine alone provides analgesia for only 2 to 2.5 hours. Most patients require further analgesia during post operativeperiod.To overcome this disadvantage various adjuvants have been tried both intrathecally and intravenously.

Recent studies have shown the efficacy of both intrathecal and IV dexmedetomidine in prolonging spinal anesthesia. Prolongation of spinal anesthesia after IV dexmedetomidine is by its supra spinal action at locus ceruleus and dorsal raphe nucleus. There are three subtypes of α 2 receptors: A, B, and C. Dexmedetomidine is a more selective α2-A receptor agonist than clonidine, with more sedative and analgesic effects. Activation of presynaptic α2-A receptors at locus ceruleus decreases norepinephrine release and causes sedative and hypnotic effects . Activation of post-synaptic α2-A receptors in CNS results in hypotension and bradycardia by decreasing sympathetic activity. Activation of post synaptic α2-Creceptors in CNS results in anxiolysis, whereas activation of post-synaptic α2-B receptors in peripheral vasculature results in transient hypertension .The study included 60 females belonging to the age group of 30 - 60 years of ASA grade 1 and 2 scheduled to undergo elective total abdominal hysterectomy. They were randomised into two groups- Group BB (received intra-thecal Bupivacaine and intravenous placebo) and Group BD (received intrathecal Bupivacaine and intravenous

Dexmedetomidine) and the effects were compared between the two groups.

The results of the clinical study are discussed under the following headings.

1, Onset of sensory and motor block 2,Two dermatomal regression time 3,Duration of sensory block and motor block.4,Degree of sedation.5,Hemodynamic stability and 6,Adverse effects ..

DEMOGRAPHIC PROFILE

The mean age (in years) of the patients in group BB was 42.33. The mean age of the patients in group BD was 44.57. The mean age of both groups were demographically comparable.

All 60 were female patients belonging to ASA grade I and II scheduled to undergo elective total abdominal hysterectomy.

DOSAGE OF ALPHA AGONIST

Dinesh C N et al (6) and Kumar S K et al (9) have used 1mcg/kg IV dexmedetomidine as loading dose over 10min followed by 0.5 mcg/kg/hr infusion till the end of surgery and found that both duration of sensory and motor block was significantly prolonged"[6,9]. "**Sangma S J et al (7)** have used 1mcg/kg IV dexmedetomidine as loading dose over 10 min followed by 0.2mcg/kg/hr infusion till the end of surgery and found that duration of motor and sensory block was significantly prolonged".[7]

Hence in our study we have chosen 1mcg/kg IV dexmedetomidine as loading dose followed by 0.5mcg/kg/hr IV dexmedetomidine as maintanence dose till end of surgery.

ONSET OF SENSORY AND MOTOR BLOCK

In our study the time of onset of sensory and motor block was rapid in Group BD (1.27 & 2.28 min) than in Group BB (2.27&3.37 min) and the difference was significant.

DURATION OF SENSORY AND MOTOR BLOCK

In our study the mean duration of sensory and motor block was longer in Group BDthan Group BB and the difference was significant.

In our study the mean duration of sensory block in the dexmedetomidine group was 337.33 minutes and in the normal saline group was 218 minutes (p value0.00). "This was similar to the study conducted by **Dinesh C N et al (6)** ,where the duration of sensory block in dexmedetomidine group was 269.8 minutes. In the study conducted by **Gupta K et al ,(8)** duration of sensory blockade in dexmedetomidine group was 259.7 minutes and in the study conducted by **Kubre J et al (13)** ,the duration of sensory block in dexmedetomidine group was 234.67 minutes."[6,8,13].

In our study the mean duration of motor block in the dexmedetomidine group was 248.33 minutes and in normal saline group was 167.67 minutes (p value 0.00)."This was similar to the study conducted by Sangma S J et al (7), where the duration of motor block in dexmedetomidine group was 263.73 minutes and in the study conducted by **Dinesh C N et al (6)**, the duration of motor block in dexmedetomidine group was 220.7 minutes[6,7]".

DURATION OF TWO DERMATOMAL REGRESSION

`In our study the duration of two dermatomal regression time was longer in Group BD than Group BB and the difference was significant. The mean duration of two dermatomal regression was 143.87 minutes in dexmedetomidine group which was longer compared to normal saline group (113.67 minutes).

In a study done in Bangalore by **Dinesh C N et al** (6), "the duration for two-dermatomal regression of sensory blockade (137.4 ± 10.9 min vs. 102.8 ± 14.8 min) was significantly prolonged in dexemedetomidine group ($P < 0.001$) than placebo group and was comparable with our study"[6].

Sangma S J et al (7) conducted a "placebo-controlled study which showed two dermatomal regression was prolonged in the dexmedetomidine group compared to the control group (294 ± 18.2 min vs. 288 ± 24.3 min, $P < 0.05$)"[7] and was concordant with our study.

DEGREE OF SEDATION

In our study the degree of sedation as assessed by Ramsay sedation scale was higher in dexmedetomidine group compared to placebo group. The average Ramsay sedation score was 3.267 in dexmedetomidine group (p value 0.00).

"In the study conducted by **Dinesh C N et al (6),** sedation scores were higher in dexmedetomidine group (4.4) compared to placebo group (2) ($p < 0.001$)"[6].

The Ramsay sedation scale was higher in dexmedetomidine group in **Kumar S K et al study (9), Tiwari D et al study (10).**

In the study conducted by **Lee M H et al (12),** in 2014 , the Ramsay sedation score was significantly higher in the D-0.5 and D-1 groups than in the control group"[12].

HEMODYNAMIC VARIABLES

In our study, dexmedetomidine group had a lower pulse rate from 15th minute to 60th minutes compared to placebo group and was similar to **Gupta K et al (8)** study which also demonstrated significant decrease in heart rate in dexmedetomidine group.

Dinesh C et al (6) and Abdallah F W et al (11), in their study also showed significant decrease in heart rate similar to our study with dexmedetomidine.

In our study, there was no significant difference in the mean arterial pressure and oxygen saturation between the two groups and was comparable with the studies done by **Kumar S K et al and Tiwari D et al (9,10).**

ADVERSE EFFECTS

In our study dexmedetomidine group 23.33% developed bradycardia compared to normal saline group 6.66% and was comparable with Dinesh C et al study "in which 33% in dexmedetomidine group developed bradycardia compared to 4% in normal saline group".Similarly **Gupta K et al** (8) in his study demonstrated significant decrease in heart rate in patients of dexmedetomidine group.

In our study, the incidence of post-op shivering was found to be lesser in the dexmedetomidine group and was comparable with study conducted by **Upadhyay S P et al (14).**

The incidence of hypotension and vomiting were same in both dexmedetomidine group and placebo group. No incidence of respiratory depression, and pruritus were found in both the groups.

CONCLUSION

The present study concludes that

1. The **onset** of sensory and motor blockades were earlier in the dexmedetomidine group.
2. The **duration** of both sensory and motor blockades were prolonged in dexmedetomidine group compared to placebo group.
3. Both groups had comparable hemodynamics.
4. The degree of sedation was better in the dexmedetomidine group when compared to placebo group.
5. The incidence of bradycardia was significantly higher in the dexmedetomidine group but it was transient and reversible with atropine.
6. There was less post-op shivering in the dexmedetomidine group than placebo group.

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