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Effect of intravenous and epidural dexmedetomidine on spinal block in lower limb and lower abdominal surgeries. A comparative study

Anaesthesiology

KEYWORDS: Dexmedetomidine, intravenous, epidural, spinal anaesthesia.

Dr. Mrinal Kanti DebBarma	Junior Resident, Department of Anaesthesiology and Critical Care, Regional Institute of Medical Sciences, Imphal-795004, Manipur, India.
Dr. Ashem Jack Meitei	Assistant Professor, Department of Anaesthesiology and Critical Care, Regional Institute of Medical Sciences, Imphal-795004, Manipur, India.
Dr. Pradipkumar Singh L	Professor, Department of Anaesthesiology and Critical Care, Regional Institute of Medical Sciences, Imphal-795004, Manipur, India.
Dr. Mithun Raj R	Junior Resident, Department of Anaesthesiology and Critical Care, Regional Institute of Medical Sciences, Imphal-795004, Manipur, India.
Dr. Ch. Rabindra Singh	Junior Resident, Department of Anaesthesiology and Critical Care, Regional Institute of Medical Sciences, Imphal-795004, Manipur, India.

ABSTRACT

Background: Dexmedetomidine, a selective α2 agonist with sedative and analgesic properties has been used to prolong duration of analgesia. **Aim**: The present study was designed to see the effect of dexmedetomidine 0.5cmg/kg of body weight given epidurally produces longer analgesia and sedation than given intravenously on hyperbaric bupivacaine spinal anaesthesia. **Materials and Methods**: Hundred patients undergoing lower abdomen or lower limb surgeries under spinal anaesthesia were selected and randomly divided into group I and group E. Immediately following spinal anesthesia, both the groups received bolus dexmedetomidine 0.5μg/kg over ten minutes followed by infusion of 0.5mcg/kg/hr through the respective allocated route of administration for the duration of surgery (i.e. Group I: i.v and group E: epidural). Time for the onset of sensory and motor block, time of loss of pain to pin prick sensation up to T10, time of sensory regression by 2 segments and duration of analgesia were recorded. Sedation scores by Ramsay Sedation Score (RSS) and haemodynamic parameters were assessed. **Results:** Time of sensory regression by two segments was significantly prolonged in the epidural group than intravenous group (257.06±15.60 min vs 184.90±22.46 min), P<0.001. Sedation for intravenous group was higher than epidural group and was statistically significant from 15 minutes onwards (P<0.05). Postoperative analgesia was significantly prolonged in epidural group (335.30±47.62 min vs 223.5±28.93 min) than intravenous group, P<0.001. **Conclusion**: Epidural infusion of dexmedetomidine prolonged the duration of post operative analgesia compared to intravenous infusion with equal dose. But easily arousible sedative effect was higher in intravenous group.

Introduction:

Post operative pain relief is a challenging problem. Prolongation of spinal analgesia not only extends the duration of surgical anesthesia but also provides post operative analgesia for considerable duration. Alpha-2 agonist like dexmedetomidine has been used as adjuvant to prolong subarachnoid block.[1,2] It possesses properties of sedation, anxiolysis and analgesia without the development of respiratory depression.[3-5] Among the few studies done earlier with different bolus doses of intravenous dexmedetomidine followed by infusion, 0.5mcg/kg[6] shown prolonged duration of spinal anaesthesia without significant side effects compared to 1mcg/kg which had shown a few significant side effects.[7] Other few more studies[8-9] on comparison between intravenous and epidural patient controlled analgesia (PCA) had shown that epidural route allows less consumption of drugs for the same level of analgesia. The present study was designed to evaluate the lower dose of dexmedetomidine (0.5mcg/kg bolus, 0.5mcg/kg/hr) given epidurally produces longer analgesia and sedation than given intravenously.

Materials and Methods:

After obtaining approval from institutional ethics committee and written informed consent from the patients, this single blinded randomized clinical study was conducted at a tertiary care teaching hospital in Imphal during September 2014 to August 2016. One hundred adult patients of American Society of Anaesthesiologists (ASA) physical status I-II aged between 18-55 years of either sex undergoing lower abdominal or lower limb orthopedic surgeries were included in the study. Patients with infection at the puncture site, hypersensitivity to drug used, diabetes, hypertension, psychiatric and neurological diseases, spinal deformity and refuse to give consent were excluded from the study. Sample size was calculated based on one study[6] which was 49 in each group taking value of 5% and power of 80% to detect a difference of minimum 30 minutes (15%) in the duration of sensory block. Rounding up we had taken 50 patients in each group. By computer generated randomization, patients were divided into two groups of 50 patients in each.

Group I patients received 0.5% hyperbaric bupivacaine (12.5mg) 2.5 ml intrathecally in L_{3-4} and intravenous (i.v) dexmedetomidine 0.5mcg/kg bolus over 10 minutes followed by 0.5mcg/kg/hr for the duration of surgery.

Group E patients received 0.5% hyperbaric bupivacaine (12.5mg) 2.5ml intrathecally in L_{3-4} and bolus epidural dexmedetomidine 0.5mcg/kg over 10 minutes followed by 0.5mcg/kg/hr in L_{2-3} space for the duration of surgery.

Study tools:

- Hyperbaric Bupivacaine (Anawin 0.5% Heavy)
- Injection Dexem (Dexmedetomidine)
- Anaesthesia workstation – Drager,
- Multiparameter monitor – Infinity Vista Xl,
- Epidural anaesthesia set for continuous infusion of drug- Perifix ONE 401 Filter set.
- Spinocane (Needle for spinal anaesthesia) B Braun, made in Germany.

One day before the surgery, preanaesthetic check up was conducted and a detailed history with complete physical and systemic examination was recorded. All routine investigations were done and checked. Patients were kept nil per oral overnight following medication with oral tablet ranitidine 150 mg plus tablet diazepam 10 mg. On arrival at operation theater, one hour before the procedure, tablet ranitidine 150 mg plus tablet metoclopromide 10 mg were

repeated orally with a sip of water. Intravenous access was established with 18G cannula and preloading was done with Ringer Lactate at 15ml/kg body weight, 30 minute before procedure. Pulse oximeter, non invasive blood pressure monitor (NIBP) & electrocardiography (ECG) were applied to each patient and baseline parameters were recorded.

Under aseptic and antiseptic precautions epidural catheter (20G) was put in left lateral position through midline approach at L_{2-3} epidural space using loss of resistance technique followed by intrathecal injection of hyperbaric bupivacaine 0.5% Heavy 2.5ml (12.5 mg) in L_{3-4} space. Depending on randomization plan dexmedetomidine 0.5mcg/kg bolus infused over 10 minutes followed by 0.5mcg/kg/hr was given intravenously or epidurally for duration of surgery. Motor blockade was assessed by modified bromage scale (0= No motor block, 1= Can flex knee, move foot but cannot raise leg, 2= Can move foot only, 3= cannot move foot or knee). Block characteristics was assessed as:-

T_1- Time of sensory onset (tingling, numbness).
T_2- Time of loss of pain to pinprick sensation up to T_{10}.
T_3- Time of maximum block height (level of dermatome remaining steady in four consecutive observations when checked every two minutes).
T_4- Time of motor block up to modified bromage Scale 2.
T_5- Time of sensory regression by two segments.
T_6- Duration of analgesia (from first intrathecal injection to first rescue analgesic).
T_7- Motor regression to modified bromage scale 1
The sedative effect was assessed and recorded using Ramsay Sedation Score (RSS)[10]

Intra operative heart rate and blood pressure (systolic, diastolic, and mean) were checked following spinal injection every two minutes for the first ten minutes, and then every five minutes till the end of surgery. Hypotension was defined as fall in systolic blood pressure more than 20% from the base line. It was corrected with incremental intravenous fluids or injection mephentermine 3mg intravenous bolus. Bradycardia was defined as heart rate < 50/min and corrected by injection atropine 0.3 to 0.6 mg intravenously.

Post operatively, pain was assessed by visual analogue scale (VAS). First rescue analgesic was given by 75mg of injection diclofenac intramuscular when the visual analogue scale (VAS) is ≥4 (0= No pain, 1-3= Mild pain, 4-6= Moderate pain, 7-10=Severe pain) or sensory regression to S_2 whichever comes earlier.

Complications like hypotension, bradycardia, nausea, vomiting, sedation were noted during the first twenty four hours post operatively and treated accordingly. Amount of analgesic and antiemetics consumed in first twenty four hours were also recorded.
Statistical analysis was performed using the Statistical Package for Social Sciences version 21 (IBM) software. Continuous variables were presented as mean±SD and for categorical variables were described as number of cases or percentages. The mean parametric data between intravenous and epidural route of administration were compared by independent sample test (t-test) and χ^2-test was applied for categorical variables. *P*<0.05 was considered as statistically significant.

Results:

Table-1: Demographic profile of the two study groups

Parameters	Route of administration		x^2-value/ t-value	P-value
	(Group I) Intravenous	(Group E) Epidural		
Sex (F:M)	40(80):10(20)	36(72):14(28)	.877	.349
Age (Yrs.)	41.76±9.52	41.98±10.68	.109	.914
Weight (Kg)	56.46±6.46	55.22±6.07	.988	.325
Surgery duration (Min.)	45.60±22.35	59.60±22.42	1.117	.267

x^2: Chi-square; P: Probability of difference due to chance factors.

The demographic data were comparable for age, sex, weight, duration of surgery which were statistically not significant (P>0.05) Table-1.

2: Mean±SD of block characteristics between two groups

Parameters	Route of administration		t-value	P-value
	(Group I) Intravenous	(Group E) Epidural		
Time of sensory onset (Sec.)	11.70±15.88	10.46±2.05	.547	.585
Loss of pain to pin prick sensation up to T10 (Sec.)	186.16±11.04	185.96±9.92	.095	.924
Time of maximum block height (Sec.)	304.20±18.58	282.50±19.17	5.747	<.001
Time of motor block up to modified bromage scale 3 (Sec.)	343.00±13.31	331.66±14.08	4.137	<.001
Time of sensory regression by 2 segments (min.)	184.90±22.46	257.06±15.60	18.654	<.001
Duration of analgesia (min.)	223.50±28.93	335.30±47.62	14.188	<.001
Motor regression to modified bromage scale 0 (min.)	190.80±21.39	242.10±11.12	15.048	<.001

t: Independent sample test; SD: standard deviation

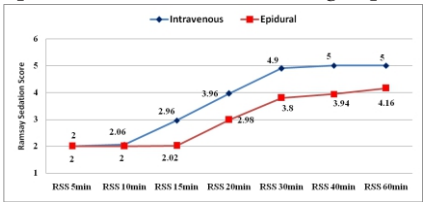
Table 2 shows that onset of sensory block in epidural route is slightly faster than the intravenous route (P=0.585) but statistically not significant. Similar insignificant difference was observed for loss of pain to pin prick sensation up to T10 (Sec) between the groups (P=0.924). The remaining block characteristics between the groups were highly significant (P<0.001). Means of time of maximum block height (Sec.) and time of motor block up to modified bromage scale 3 (Sec.) were longer in intravenous group than that of the epidural group. On the contrary for time of sensory regression by 2 segments (min.), Duration of analgesia (min.) and motor regression to modified bromage scale 0 (min.) the former group has less mean times when compared with the corresponding figures of latter group.

Table 3: Mean±SD of Ramsay sedation score (RSS)

Parameters	Route of administration		t-value	P-value
	(Group I) Intravenous	(Group E) Epidural		
RSS at 5 min.	2.00±0	2.00±0		
RSS at 10 min.	2.06±.240	2.00±0	1.769	.080
RSS at 15 min.	2.96±.198	2.02±.141	27.322	<.001
RSS at 20 min.	3.96±.198	2.98±.247	21.913	<.001
RSS at 30 min.	4.90±.364	3.80±.404	14.299	<.001
RSS at 40 min.	5.00±0	3.94±.240	31.244	<.001
RSS at 60 min.	5.00±0	4.16±.370	16.039	<.001

The mean score of sedation for intravenous route was higher than that of epidural route which was found true in all the stages, under consideration in the present study (Table 3). Nevertheless, the variations were meager at 5th and 10th minutes in the beginning and at 60th minute on the later stage (Fig 1).

Fig-1. Comparison trend of RSS between two groups



Thus in the early two stages, there was no significant difference between the groups whilst a highly significant difference of means was noticed for each remaining stage between the groups (p <0.001).

Table 4: Mean±SD comparison of heart rate (HR) between two groups

Parameters	Route of administration		t-value	P-value
	(Group I) Intravenous	(Group E) Epidural		

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Pre-op HR	81.82±10.680	84.34±10.64	1.182	.240
HR at 2 min	79.22±10.50	81.68±10.38	1.177	.242
HR at 4min	75.38±9.73	80.16±10.03	2.417	.017
HR at 6min	71.84±10.25	78.02±9.21	3.169	.002
HR at 8min	66.68±8.86	74.16±9.35	4.104	<.001
HR at 10min	64.46±8.78	72.36±8.96	4.452	<.001
HR at 15min	66.58±10.12	71.84±9.81	2.638	.010
HR at 20min	66.02±8.02	72.62±9.70	3.706	<.001
HR at 30min	68.50±6.24	73.98±9.36	3.443	.001
HR at 40min	68.42±6.90	73.54±9.15	3.159	.002
HR at 50min	69.52±5.83	74.58±8.66	3.426	.001
HR at 60min	69.44±7.31	75.52±8.80	3.756	<.001

Basal heart rate was comparable between the two groups and statistically not significant. Intra-operatively there was clinically and statistically significant decrease in heart rate in intravenous group from 4 min and persisted till last observation when compared to epidural group (Table-4).

Table-5: Haemodynamic parameters of the study groups

Time Intervals	SBP variation (Mean±SD)			DBP variation (Mean±SD)			MAP variation (Mean±SD)		
	(Group I) Intravenous	(Group E) Epidural	P value	(Group I) Intravenous	(Group E) Epidural	P value	(Group I) Intravenous	(Group E) Epidural	P value
Pre op	125.98±11.89	127.08±10.99	.632	77.44±8.05	81.02±8.39	.032	93.62±8.61	96.37±8.47	.110
2 min	107.90±12.32	106.92±12.03	.688	68.02±10.81	71.02±12.64	.205	81.31±10.38	82.99±10.92	.434
4 min	107.02±8.91	109.14±11.85	.315	64.38±10.27	68.98±10.53	.029	78.59±9.21	82.37±10.41	.058
6 min	114.62±9.01	115.40±8.96	.665	70.90±8.15	72.80±6.33	.196	85.47±7.67	87.00±7.07	.303
8 min	109.82±11.47	114.60±8.36	.019	66.98±9.98	72.72±6.84	.001	81.26±10.21	86.68±7.16	.003
10 min	104.98±10.40	108.26±10.85	.126	65.02±11.58	67.32±10.23	.295	78.34±9.78	80.97±9.79	.183
15 min	104.80±7.19	108.94±10.63	.025	62.02±7.59	66.54±9.35	.009	76.28±7.01	80.67±9.28	.009
20 min	105.06±7.42	107.12±8.73	.207	62.82±6.75	64.94±8.23	.162	76.90±6.30	79.00±7.77	.141
30 min	105.96±6.99	107.58±7.14	.255	63.42±6.94	64.94±8.53	.331	77.60±6.09	79.15±7.45	.256
40 min	107.58±7.82	108.58±8.39	.539	63.82±8.04	66.90±8.43	.065	78.41±7.02	80.79±8.00	.116
50 min	108.42±6.07	109.08±6.33	.596	66.48±6.82	67.42±6.63	.487	80.46±6.30	81.31±6.43	.508
60 min	108.74±5.14	110.82±7.09	.097	67.60±5.72	69.40±6.96	.161	81.31±5.33	83.21±6.92	.129

Pre op (Pre operative baseline); SBP (systolic blood pressure); DBP (diastolic blood pressure); MAP (Mean arterial pressure)

Table-5 shows that haemodynamic changes were statistically significant only at 8th and 15th minutes (P<0.05) while the remaining were not statistically significant. Thus the route of administration adopted in this study had minimal role towards the regulation of blood pressure.

The duration of post operative analgesia was significantly prolonged in group E (335.50±28.93 min) compared to group I (223.50±47.62 min), P<0.001 Fig-2.

We observed that (table-6) group I had 6 (12%) patients vomiting as against 3 (6%) patients for epidural group but statistically not significant (P=0.295). Rescue analgesic requirement in first 24 hours of post operative period was significantly less in epidural group than intravenous group (P<0.001).

Fig- 2: Comparison of mean duration of postoperative analgesia

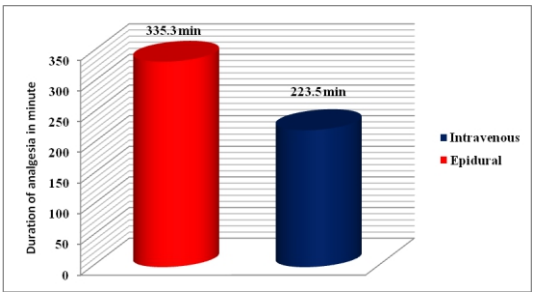

Table-6 Comparison of incidence of nausea & vomiting and rescue analgesic

Parameters		Route of administration		x^2-value	P-value
		Group I	Group E		
Postoperative nausea, vomiting in first 24hrs	No vomiting	44(48.4%)	47(51.6%)	1.099	.295
	Vomiting	6(66.7%)	3(33.3%)		
Rescue analgesic in the first 24hrs	1 time medication	16(30.2%)	37(69.8%)	20.111	<.001
	2 time medication	23(65.7%)	12(34.3%)		
	3 time medication	11(91.7%)	1(8.3%)		

Discussion: Effective post operative analgesia is necessary to provide subjective comfort and alleviate the suffering in patients undergoing surgery. Dexmedetomidine as adjunct to intrathecal bupivicaine given by epidurally or intravenously have shown to prolong the duration of block along with sedative and analgesic effect.[1,2,11] In our study dexmedetomidine 0.5mcg/kg/hr was infused in two different routes, (intravenous and epidural) after bolus dose of 0.5mcg/kg infused over 10 minutes to produce sedation and analgesic for the duration of surgery performed under spinal bupivacaine anesthesia. From the results of our study, we observed that there was significant prolonged duration of post operative analgesia in epidural group than the intravenous group with more sedative effect in intravenous group than that of epidural group. Negligible side effects like hypotension and bradycardia was seen among few individuals but was more in intravenous group.

Our finding of prolongation on duration of post operative analgesia when dexmedetomidine was given as bolus at the dose of 0.5mcg/kg followed by infusion of 0.5mcg/kg/hr was in accordance with those of Harsoor SS et al [6] who concluded that dexmedetomidine given during subarachnoid block had prolonged sensory and motor block with satisfaction arousable sedation without causing respiratory depression.

Again, our findings of prolongation of mean duration of postoperative analgesia in the epidural group compared to the intravenous group (335.30 ± 47.62 vs 223.5 ± 28.93) was in accordance with those of Mann C et al[8] who concluded the patient controlled epidural analgesia has got better relief compared to the patient controlled analgesia given by intravenous route.

We also observed that prolongation of sensory regression by two segments in the epidural group compared to intravenous group (257.06 ± 15.06 vs 184.90 ± 22.46) was in accordance with those of Kanazi GE et al[2] who concluded that dexmedetomidine when added to intrathecal bupivacaine produce prolongation in the duration and sensory block with preserved haemodynamics.

In our study rescue analgesics required by the patient in the first 24 hours of postoperative period was less with the epidural group compared to intravenous group. It was in accordance to the Bernard et al[9] who concluded that epidural administration allows for a reduction in dose requirement.

In our study, though we observed all the patients were sedated properly attaining Ramsay Sedation Score 3, 4, and 5, they were easily arousable and alerted when stimulated verbally or with light touch. It

was found that the mean score of epidural group which starts from the 15th minute of administration and is statistically significant. This observation was similar to the results found during the study conducted by Belleville JP et al.[12]

Nausea and vomiting during the first 24 hours post operatively were more with intravenous group (12% vomiting) than epidural group (6% vomiting). In our study we had observed a very meager change in blood pressure and heart rate. This is comparable with the study conducted by Song J et al[7] using intravenous dexmedetomidine at 1µg/kg bolus and produced bradycardia, hypotension and decreased cardiac output despite increasing the duration of spinal anesthesia. On contrary we had avoided these complications by using lower dose (0.5mcg/kg).

The result obtained in our study demonstrates that administration of dexmedetomidine in epidural route prolongs the sensory and motor block along with duration of postoperative analgesia whereas the sedative effect of intravenous dexmedetomidine is higher than the epidural group when used in spinal anesthesia. In addition dexmedetomidine provides good sedation and minimal side effects in both the groups.

Limitations: We have included many types of surgeries and the intensity of pain may differ depending upon the type of surgery. The initial intravenous or epidural bolus of 0.5µg/kg dexmedetomidine is given over 10 minutes after intrathecal injection of bupivacaine limiting the intra-operative assessment of analgesia.

Conclusion: We conclude that epidural administration of dexmedetomidine prolonged the duration of postoperative analgesia compared to intravenous group with equal dose. The sedative effect though easily arousable was higher in the intravenous group. Side effects like intraoperative hypotension, bradycardia and postoperative nausea vomiting although negligible, was found comparatively less in the epidural group.

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