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DEXMEDETOMIDINE AND BUPRENORPHINE AS ADJUVANT TO SPINAL ANAESTHESIA - A COMPARATIVE STUDY

B. Maharani[1], M. Sathya Prakash[2], Paramesh Kalaiah[1], N.C. Elango[2]

[1]Department of Pharmacology, Annapoorana Medical College and Hospitals, Salem, Tamil Nadu, India
[2]Department of Anaesthesiology, Annapoorana Medical College and Hospitals, Salem, Tamil Nadu, India

E-mail of Corresponding Author: drkarthikrani@gmail.com

ABSTRACT

Background: Dexmedetomidine – an α_2 agonist, Buprenorphine – an opioid receptor agonist and antagonist can be safely used as adjuvants to spinal anaesthesia. There are no studies comparing dexmedetomidine and buprenorphine when used as adjuvants in subarachnoid block.

Aim: The objectives of the study: To evaluate and compare the onset and duration of sensory and motor block, perioperative analgesia, side effect profile of dexmedetomidine and buprenorphine when used as adjuvant to bupivacaine in spinal anaesthesia for surgeries below the level of umbilicus.

Materials and methods: Sixty patients of ASA I & II scheduled for lower abdominal & lower limb surgeries were randomly allocated in to two groups (group A & group B) and received the following drugs

- Group A – 15 mg of 0.5% Hyperbaric bupivacaine + 10 µg of Dexmedetomidine
- Group B – 15 mg of 0.5% Hyperbaric bupivacaine + 60 µg of Buprenorphine.

Sensory and motor blockade characteristics (onset time, time to reach maximum level and regression), time for rescue analgesia and side effects were recorded. Observed parameters were statistically analyzed by using independent sample't' test (SPSS version 12). $P<0.05$ was considered statistically significant.

Results: Addition of dexmedetomidine as adjuvant to bupivacaine had significantly shortened the onset of sensory blockade (100.50±31.74 and 122.13±36.25, $P<0.05$), prolonged the duration of motor and sensory block ($P<0.001$, $P<0.001$ respectively) and had postponed the time for first analgesic request (295.83±93.21 and 238.27±110.36, $P<0.05$) without any side effects when compared to buprenorphine ($P<0.05$, $P<0.001$).

Conclusion: 10µg of dexmedetomidine seems to be a better alternative to 60 µg of buprenorphine when added as adjuvant to bupivacaine in spinal block for lower abdominal and lower limb surgeries below the level of umbilicus.

Keywords: Dexmedetomidine, Buprenorphine, Bupivacaine, Lower abdominal surgery.

INTRODUCTION

Spinal Anaesthesia (Subarachnoid block) is the most commonly used anaesthetic technique for wide variety of elective and emergency surgical procedures below the level of umbilicus. It is very economical, safe and easy to administer.[1] The common problems with lower abdominal surgeries under spinal anaesthesia are visceral pain, nausea and vomiting.[2] This can be overcome by the addition of adjuvant to local anaesthetics for subarachnoid block. Various adjuvants like clonidine, dexmedetomidine (α_2 agonist), morphine, tramadol, fentanyl, buprenorphine (Opioids) and magnesium

(NMDA antagonist) are added to increase the duration of sensory and motor block, to improve intraoperative analgesia, to delay the regression of sensory block and postpone the time to first analgesic request.[3] But there are certain advantage and disadvantages with each adjuvant. Hence studies are conducted to identify safer and effective spinal adjuvant.

Buprenorphine is μ and κ opioid receptor mixed agonist & antagonist. Buprenorphine when given intrathecally has analgesic action by its action on opioid receptors.[4] But side effects like delayed respiratory depression, pruritis and vomiting had made the need to find an alternative analgesic devoid of the side effects and better clinical efficacy.[5]

Dexmedetomidine a novel drug is being used in anaesthetic practice for its sedative, anxiolytic, analgesic, neuroprotective and anaesthetic sparing effect. It has additional advantages like minimal respiratory depression, cardioprotection, neuroprotection and renoprotection.[6] Dexmedetomidine prolongs motor and sensory block when used as adjuvant to local anaesthetic for spinal anaesthesia.[7] It is used in the dose of 3 to 15 mcg as adjuvant to spinal anaesthesia. [8] There are no studies comparing buprenorphine and dexmedetomidine when used as adjuvants in subarachnoid block. Hence this present study was carried out with the following objectives:

Aim: To evaluate and compare the onset and duration of sensory and motor block, perioperative analgesia, side effect profile of dexmedetomidine and buprenorphine when used as adjuvant to bupivacaine in spinal anaesthesia for surgeries below the level of umbilicus.

MATERIALS AND METHODS

The study was approved by institutional ethical committee, written informed consent was obtained from the patients participating in the study. This was a randomized prospective interventional study. Convenient sampling method was followed and the study was conducted on 60 patients of either sex, belonging to ASA-I & II (American Society of Anesthesiologists physical status), between the age group of 18-60 years who were enrolled for lower abdominal and lower limb surgeries. The patients with history of hypertension, heart disease, renal failure, sedative drug consumption, allergic to the local anaesthetics and patients belonging to ASA III & IV, refusal to spinal anaesthesia were excluded from the study. The patients were randomly allocated into two groups (Group A & B) of 30 each. Group A received 15mg of hyperbaric bupivacaine with 10 μg of dexmedetomidine and Group B received 15 mg of hyperbaric bupivacaine with 60 μg of buprenorphine. All patients were kept nil by mouth for 8 hours prior to surgery. The patients were not premedicated as it may interfere with the study parameters.

The baseline blood pressure, pulse rate, respiratory rate were observed. IV access was secured with 18gauge cannula. After preloading with ringer lactate solution (10ml/kg of Body weight), the patients were placed in right lateral position and lumbar puncture was performed at L3-L4 space with 26gauge spinal needle with all aseptic precautions. Ensuring free flow of C.S.F, the appropriate drug for that designated group was injected and the patients were made to lie down in supine position. Blood pressure, pulse rate and Spo2 were recorded immediately after subarachnoid block and thereafter every 5 minutes till the end of surgery. Oxygen was administered through a face mask if the pulse oximetry reading decreased below 95%. Intraoperative hypotension was considered to be present whenever systolic blood pressure decreased to less than 20% of baseline and it was managed with bolus of I.V fluids and incremental doses of I.V ephedrine. Bradycardia defined as heart rate less than 50 bpm and was treated with I.V atropine. Any untoward incident and side effects like nausea, vomiting,

respiratory depression, pruritis and shivering during the study period were carefully observed, recorded and managed symptomatically. Onset of sensory block was assessed by loss of pinprick sensation to 23gauge hypodermic needle and dermatomal levels were tested. Modified Bromage scale (0- No block, 1- Inability to raise extended leg, 2- Inability to flex knee, 3- Inability to flex ankle and foot) was used to assess the motor blockade. The following parameters were observed and recorded: onset of sensory blockade to T10 level, maximum sensory block level, time for maximum level sensory block, onset of motor blockade to modified bromage 3, time for complete motor block, regression of motor block to modified bromage 0, regression of sensory block to S1 level, duration of sensory and motor block. Sedation was graded according to Ramsay sedation score. Post operative pain and time for rescue analgesia were recorded by using Visual Analogue Scale. Injection Diclofenac 100mg was given intramuscularly as rescue analgesic. No intraoperative sedation was given, as the patients were comfortable throughout the surgery.

Statistical analysis was done by SPSS version 12. Parametric data were reported as arithmetic mean ± standard deviation and analyzed by independent sample‘t’ test. The comparison was studied using Chi-square or the Fisher’s exact test as appropriate, with P value reported with the 95% confidence interval. $P<0.05$ was considered statistically significant.

RESULTS

The groups were comparable with respect to age, weight, gender, height, ASA physical status and the differences among them were not statistically significant [Table -1]. There was no significant difference in the type of surgery [Table-2]. Baseline preoperative vital parameters were comparable and there was no statistical difference between the groups [Table-3]. Sensory and motor block parameters were represented as mean ± S.D [Table-4]. Highest level of block (T2) achieved with dexmedetomidine (4nos) was statistically significant than buprenorphine (2nos) ($P< 0.043$). Sensory and motor block parameters achieved with dexmedetomidine was statistically significant than with buprenorphine, except with onset of motor blockade ($P=0.740$, NS) [Table-4]. The duration of analgesia was significantly prolonged with addition of dexmedetomidine as compared to buprenorphine (295.83±93.21min and 238.27±110.36 min respectively, $P=0.033$).

Figure: 1 depicts the comparison of the side effects of dexmedetomidine and buprenorphine. Nausea, vomiting and respiratory depression was significantly present only in group B receiving buprenorphine ($P\leq 0.05$). It had also produced bradycardia, pruritis and shivering which are not significant. Intraoperative hypotension was observed in both the groups but it was more in dexmedetomidine group which was not statistically significant ($P=0.13$, NS). Intraoperative hypotension was managed with ephedrine and bradycardia was managed with atropine. Both the group patients were arousable throughout the surgery. The incidence of residual neurological deficit, post-dural puncture headache or transient neurological symptoms during the postoperative follow up was nil in both groups.

DISCUSSION

The results of the present study had shown that the addition of dexmedetomidine as adjuvant to bupivacaine in spinal anaesthesia had significantly shortened the onset of sensory block, prolonged the duration of motor and sensory block and had postponed the time for first analgesic request when compared to buprenorphine. Various animal and human studies were conducted with intrathecal dexmedetomidine and buprenorphine without any postoperative neurological deficits. [9,10]

Gupta et al., had found the superiority of dexmedetomidine in sensory and motor block characteristics when added as adjuvant to ropivacaine intrathecally.[11]

The mechanism of action responsible for prolongation of motor and sensory blockade with intrathecal dexmedetomidine is not well known. It was proposed that, Dexmedetomidine acts as an agonist on α_{2}- adrenoreceptors located in the pre-synaptic C-fibres and post-synaptic dorsal horn neurons in the spinal cord. When it is given intrathecally, it produces analgesia by depressing the release of C-fiber excitatory nociceptive transmitters (glutamate & substance-P) and by hyper polarization of post-synaptic dorsal horn neurons. [12-15] This may also be responsible for higher level of block (T2) achieved with dexmedetomidine when compared to buprenorphine. α_2-adrenoreceptor agonist by binding to α_2 receptors in motor neuron of dorsal horn of spinal cord inhibits the release of excitatory transmitter and prolongs the duration of motor blockade.[16]The most common side effect with α_2 adrenoreceptor agonist is bradycardia and hypotension. The sympatholytic effect through activation of pre-synaptic α_2-adrenoreceptor is responsible for hypotension. [17] In the present study, dexmedetomidine produced manageable and not significant systolic hypotension. The probable reason is, intrathecal administration of drug produces less systemic side effects than parenteral administration. Studies done by Hall JE et al., and Ananta RE et al., have shown dexmedetomidine also has anaesthetic sparing and anaesthesia potentiating effect.[18, 19]

Various studies have demonstrated that addition of intrathecal buprenorphine to bupivacaine as spinal adjuvant produces early onset, longer duration and better quality of analgesia than bupivacaine alone. [4, 20] Pharmacological actions and side effects of buprenorphine are through activation of opioid receptors. In the present study, we observed sensory block characteristics of buprenorphine were less significant than dexmedetomidine adjuvant and also dexmedetomidine has added advantage of prolongation of motor block and post operative analgesia. Buprenorphine has produced statistically significant side effects like nausea, vomiting and respiratory depression. The rapid onset of sensory block and prolonged duration of sensory and motor blockade, long duration of postoperative analgesia with absence of systemic side effects achieved with 10µg of dexmedetomidine combined with bupivacaine for spinal anaesthesia, suggests that the drug may be particularly useful in surgeries where a prompt onset and long duration of analgesia is required.

CONCLUSION

10µg of dexmedetomidine seems to be a better alternative to 60 µg of buprenorphine when added as adjuvant to bupivacaine in spinal block for lower abdominal and lower limb surgeries. The faster onset of sensory blockade, prolonged duration of analgesia, sensory and motor block in the postoperative period, stable cardiovascular parameters and devoid of respiratory depression, nausea, vomiting and pruritis makes dexmedetomidine a very effective adjuvant in regional anaesthesia.

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Table – 1: Characteristics of participants

Physical characteristics	Group – A (range)	Group –B (range)	*P Value
Age (yrs)	46.13±9.737 (22-60)	46.07±7.395 (29-57)	0.998**
Weight(kg)	60.40±8.540 (45-80)	57.07±7.287 (45-78)	0.105**
Sex(M:F)	15:15	10:20	0.197**
Height(cm)	157.50±4.385	155.80±4.012	0.128**
ASA(I:II)	14:16	6:24	0.27**

η =30; Values are mean±SD; ASA: American society of Anaesthesiologist physical status;
* - P value < 0.05 significant; ** - P value – Not significant

Table -2: Type of surgery

Type of surgery	Group A	Group B	*P Value
Total abdominal hysterectomy	7	9	-
Lower limb surgery	5	8	-
Hernia repair	9	6	-
Vaginal hysterectomy	4	2	-
Open appendicectomy	1	1	-
Tubal recanalisation	2	2	-
Cystectomy	1	1	-
Excision of ulcer + Split Skin grafting	1	1	0.946**

η =30; *P value < 0.05 significant, ** - P value for type of surgery – Not significant

Table-3: Preoperative vital parameters of study groups

Vital parameters	Group – A (range)	Group –B (range)	*P Value
Heart rate	80.67±12.217 (62-110)	83.57±15.917 (66-122)	0.475**
Systolic blood pressure	126.60±9.298 (105-140)	128.80±9.286 (110-140)	0.231**
Diastolic blood pressure	79.23±5.469 (66-88)	81.53±5.551 (70-88)	0.109**

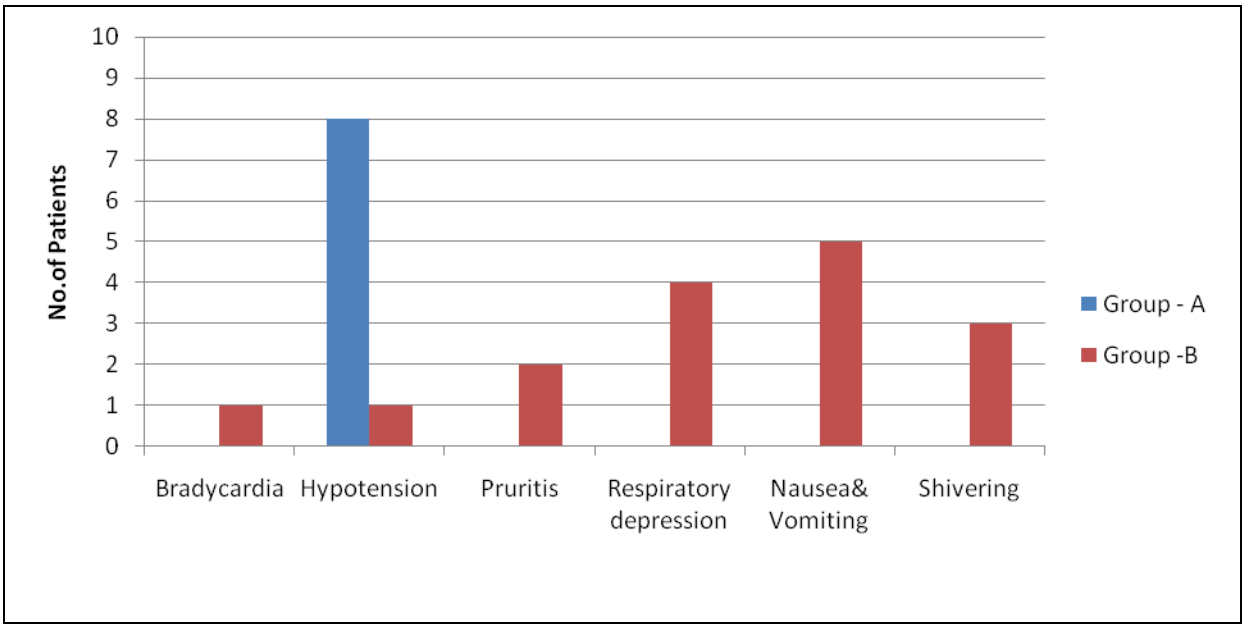
η =30; Values are mean±SD; *P value < 0.05 significant, ** - P value – Not significant

Table-4: Sensory block & Motor block parameters of study groups

Sensory & motor block characteristics in minutes	Group A	Group B	P*Value
Onset of sensory blockade to T_{10}	1.67±0.52	2.04±0.60	0.017*
Time for maximum level of sensory block	4.10±1.06	6.07±3.42	0.004*
onset of motor blockade to modified bromage 3	3.56±1.13	3.66±1.19	0.740***
Time for complete motor block	4.80±0.76	5.43±1.25	0.021*
Time for regression of motor block to modified bromage 0	345.67±48.45	270.63±73.67	<0.001**
Time for regression of sensory block to S1	377.50±48.54	304.60±75.69	<0.001**
Duration of sensory block	375.83±48.59	302.57±75.74	<0.001**
Duration of motor block	342.11±48.67	266.98±73.47	<0.001**
Time for rescue analgesia	295.83±93.21	238.27±110.36	0.033*

η =30; Values are mean±SD; *P value < 0.05 significant, ** P value < 0.001 very highly significant; *** - Not significant (NS)

Figure 1: Side effects of dexmedetomidine (group A) and buprenorphine (group B)



X – axis – side effects, Y – axis – No of patients (η =30)