COMPARISON OF DEXMEDETOMIDINE, BUPRENORPHINE AND FENTANYL AS AN ADJUVANT TO BUPIVACAINE DURING SPINAL ANAESTHESIA FOR HEMIARTHROPLASTY

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ABSTRACT

BACKGROUND

Opioids such as fentanyl or buprenorphine are being added as adjuvant to local anaesthetic for spinal anaesthesia. Dexmedetomidine, a new α_2 agonist is being tried as an adjuvant in the recent times.

MATERIALS AND METHODS

The patients were randomised into three Groups (n=30 each) by closed envelope technique. Patients in Group 1 received 10 µg fentanyl with 15 mg of 0.5% hyperbaric bupivacaine, Group 2 received 15 mg of 0.5% hyperbaric bupivacaine supplemented with 30 µg of buprenorphine and Group 3 received 15 mg of 0.5% hyperbaric bupivacaine plus 5 µg dexmedetomidine intrathecally. The time to reach maximum sensory and motor level, the regression time of the same, any adverse effects were recorded. Data were analysed using chi-square test or Fisher's exact test for categorical data and analysis of variance for continuous data. A value of $P<0.05$ was accepted as statistically significant.

Settings and Design- The study was conducted in a prospective, randomised and double-blind manner. It included ninety American Society of Anaesthesiologists class I and II patients undergoing hemiarthroplasty under spinal anaesthesia.

RESULTS

In this study, the patients in dexmedetomidine group showed significantly longer duration of motor block (240±20 mins.) and sensory blockade (180±22.2 mins.) compared to other groups, which is statistically significant (P=0.0001 and P=0.006, respectively). The time to first request of analgesic postoperatively was also longer (260±30.2) in dexmedetomidine group when compared with other groups (P=0.0001). Haemodynamic parameters were stable and there were no complications in any group.

CONCLUSIONS

We concluded that intrathecal dexmedetomidine (5 µg) with bupivacaine provides significantly longer duration of sensory and motor blockade and longer duration for first request of analgesia in the recovery than intrathecal buprenorphine (30 µg) or fentanyl (10 µg) with bupivacaine for spinal anaesthesia for hemiarthroplasty.

KEYWORDS

α_2-Adrenoreceptor Agonist, Bupivacaine, Buprenorphine, Dexmedetomidine, Fentanyl, Spinal Anaesthesia.

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BACKGROUND

Spinal anaesthesia is the preferred regional anaesthesia technique for operations on the lower limbs[(1),(2)] because it preserves respiration, consciousness while providing adequate analgesia and muscle relaxation. These advantages can be undermined when local anaesthetic alone is used for spinal anaesthesia because of its shorter duration of action.[(2),(3)]

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Many adjuvants are being tried and some are effective to prolong the anaesthetic and analgesic effect of local anaesthetic. Fentanyl and buprenorphine have been proved as effective agents to improve the quality of spinal anaesthesia.[(2),(4)] Dexmedetomidine, a selective α_2-adrenoreceptor agonist has been approved for analgesia and intravenous sedation in critical care unit.[(5),(6)] When added intrathecally, it acts on the α_2 receptors on the dorsal horn cells and decrease the sympathetic neurotransmitter release. The duration of motor block is increased by binding to motor neurons in the spinal cord.[(7),(8),(9),(10)] This study is aimed to evaluate the effects of adding dexmedetomidine, buprenorphine and fentanyl to intrathecal hyperbaric bupivacaine on the onset time, duration of motor and sensory block, intraoperative haemodynamic parameters, postoperative analgesia and complications.

MATERIALS AND METHODS

Ninety patients of either sex aged between 20-50 years belonging to American Society of Anaesthesiologists (ASA) Class I and II scheduled for hemiarthroplasty surgery under subarachnoid block at P.E.S. Institute of Medical Sciences, Kuppam, were enrolled in this prospective, randomised and double-blinded study. Patients with any contraindication to spinal anaesthesia, ischaemic heart disease, heart blocks, hypertension, renal disorders and severe liver disease, pregnant patients, chronic alcoholics and any drug abusers were excluded from the study. The preferred anaesthesia technique, the Visual Analogue Scale (VAS) for pain and other protocols were explained to the patients preoperatively and informed written consent was taken. In the operating room, an 18G intravenous cannula was inserted on the dorsum of the hand preloaded with 8 mL/kg Ringer's lactate solution.

Electrocardiogram, pulse oximeter to monitor heart rate and oxygen saturation and noninvasive arterial pressure were applied. Patients were randomised (closed envelope technique) into three equal groups (n=30 each). An anaesthesia resident not involved in the study prepared all the drug combinations, thus the blind nature of the study was maintained and the study drug is given according to allocated group as given below:

- Group 1: Received 15 mg of 0.5% hyperbaric bupivacaine plus 10 µg of fentanyl.
- Group 2: Received 15 mg of 0.5% hyperbaric bupivacaine plus 30 µg of buprenorphine.
- Group 3: Received 15 mg of 0.5% hyperbaric bupivacaine plus 5 µg of dexmedetomidine.

Lumbar puncture was performed under strict aseptic precaution in the sitting position as followed. After infiltrating with local anaesthetic, a 25G Quincke type spinal needle was inserted at L_3-L_4 or L_4-L_5 space when free flow of CSF was confirmed. The study drug is injected, spinal needle was withdrawn and the patients were put in the supine position. Oxygen 4 L/mins. by face mask was administered to all the patients. After the completion of surgery, all patients were transferred to postoperative care unit where the above said parameters are further evaluated and discharged to the ward after complete reversal of spinal block.

The Demographic Data of the Patients

Age (years), Sex, Weight (kg), Height (cm) and ASA physical status were noted. Haemodynamic parameters: Heart rate, mean arterial pressure were recorded before the procedure. After performing the block, the mean arterial pressure and heart rate were recorded every 5 minutes for the first 20 minutes and then every 15 minutes intraoperatively till the patient is discharged from the recovery room. Hypotension was considered when systolic blood pressure decreased by more than 20% from baseline or a fall below 90 mmHg, it was treated with bolus intravenous infusion of normal saline 250 mL and incremental doses of intravenous ephedrine 5 mg as required. Bradycardia was defined as heart rate ≤50 beats/mins., it was treated with 0.6 mg of intravenous atropine.

Total number of patients who required atropine or vasopressor (Ephedrine) in the intraoperative period were recorded. Sensory block levels were tested bilaterally along the mid axillary line using pinprick test every minute for the first 15 mins. or until desired level of T10 was obtained and every 5 mins. until the maximum sensory level was obtained. Time to reach the maximum sensory level and time for regression of sensory blockade to S_1 level were recorded. The motor block was assessed and recorded using modified Bromage Scale[11],[12] every 2 minutes for the first 10 minutes and every 5 minutes until modified Bromage score 3 is reached and time to reach Modified Bromage (MB) score 3 was recorded.

- MB Score 0 = The patient is able to move the hip, knee and ankle;
- MB Score 1 = The patient is unable to move the hip, but not knee and ankle;
- MB Score 2 = The patient is unable to move the hip and knee, but not ankle;
- MB Score 3 = The patient is unable to move the hip, knee and ankle.

Surgery was allowed once the desired level of T10 was achieved. The motor blockade duration was defined as the time interval from the intrathecal injection of drug to regress of motor block to modified Bromage score 0 was assessed and recorded.

Sedation Levels were Assessed Using Ramsay Sedation Score[13]

- Score 1 = Patient anxious, agitated or restless;
- Score 2 = Patient cooperative, oriented and tranquil alert;
- Score 3 = Patient drowsy, but responsive to commands;
- Score 4 = Asleep, but with brisk response to glabellar tap or tactile stimulation;
- Score 5 = Asleep with a sluggish response to light glabellas tap or tactile stimulation; and
- Score 6 = Asleep and no response.

The postoperative pain scores were recorded for 24 hours at 1, 6, 12, 18 and 24 hours using Visual Analogue Scale (VAS).[14] Time from the end of surgery to the time of first request for analgesia was recorded. Number of patients who required rescue postoperative analgesia (Tramadol hydrochloride 1 mg/kg intravenous) in 24 hours were recorded. Postoperative complications such as sedation, hyperglycaemia, hypotension, pruritus if present were attended and recorded.

Statistical Analysis

SPSS 15 was used for statistical analysis. Pilot study done showed that for 30 minutes increase in the duration of sensory blockade among the groups required 30 patients per group such that the alpha error will be 0.05 and power will be 0.8. Data were given as means and Standard Deviation (SD), medians and ranges. Chi-square and Fisher's exact tests were used for categorical data like (Sex, ASA class,

nausea/vomiting, use of additive analgesia, hypotension and bradycardia). ANOVA test was used for continuous data like (Age, Duration of surgery).

P value <0.05 is taken as significant in the limit of 95% confidence interval.

RESULTS

All the ninety patients who participated completed the study. There was no statistically significant difference observed with respect to patient's demographic data such as Age, Weight, Height, Sex, ASA status and Duration of Surgery among the three groups (Table 1).

Variables	Group 1	Group 2	Group 3	P value
Age (Years)	44.7±12	41±15	44±12	0.947
Height (Centimetres)	156±3	157±3.3	156±4	0.998
Weight (Kilograms)	64±10.2	62±10	60±8	0.960
Gender (Male/Female)	20/10	19/11	18/12	0.968
ASA Grade (1/2) n	24/6	22/8	21/9	0.942
Duration of Surgery (Minutes)	90±10	96±12	98±8	0.909

Table 1. Patient Characteristics and Other Data in the Studied Groups

Data presented as mean±standard deviation.

Regarding the spinal block characteristics (Table 2), the study groups showed no significant differences in the highest sensory block level reached and the time taken to reach the highest sensory block level (P=0.494). However, the time to regress sensory block level to S_1 was longer in Group 3 (180±22.2 mins.) when compared with Group 1 (110±14.5 mins.) and Group 2 (140±14.5 mins.), which is statistically highly significant (P=0.006). Motor blockade time to reach the modified Bromage 3 was lower in Group 3 compared to the other groups, but not statistically significant (P=0.628) and the motor block regression time to modified Bromage 0 was statistically extremely significantly (P=0.0001) longer in Group 3 (240±20 mins.) when compared with Group 1 (120±18.2 mins.) and Group 2 (200.2±18.4 mins.). The time to first request for analgesia was longer in Group 3 (260±30.2 mins.) than Group 1 and Group 2 (130±20 and 210±22.4, respectively).

Variable	Group 1	Group 2	Group 3	P value
Highest Sensory Block Level Reached	T4 (3-6)	T5 (4-6)	T4 (3-6)	0.9488
Time to Reach Highest Sensory Block Level (mins.)	12±5	16±4	9±4	0.494
Sensory Block-Time To Regression to S_1 (mins.)	110±14.5	140±20.2	180±22.2	0.006*
Motor Block-Time To Reach Modified Bromage 3 (mins.)	7.0±1.6	9±1.4	5.0±1.4	0.628
Motor Block Regression to Modified Bromage 0 (mins.)	120±18.2	200.2±18.4	240±20	0.0001*
TFA (mins.)	130±20	210±22.4	260±30.2	0.0001*

Table 2. Showing Spinal Block Characteristics of Patients in Three Groups

Data were expressed as mean±standard deviation, median and range, mins: minutes, TFA: Time to first request of postoperative analgesic, T: thoracic, S: sacral, *P values <0.05 is statistically significant.

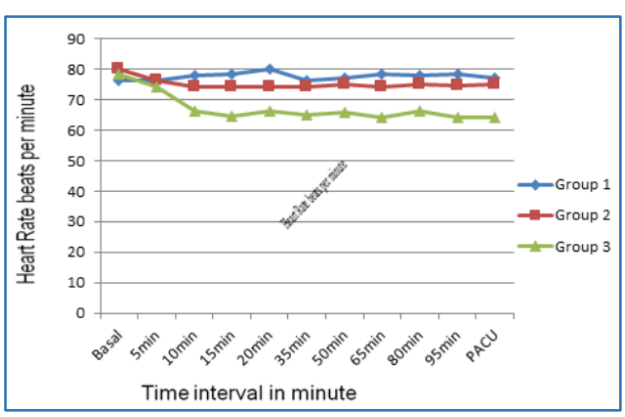

Figure 1. Showing Heart Rate Variations in Three Groups

There is no statistically significant variation in heart rate of patients in 3 Groups (P>0.05) (Figure 1). With regards to intraoperative mean arterial blood pressure, the study groups showed no significant differences (P>0.05) (Figure 2).

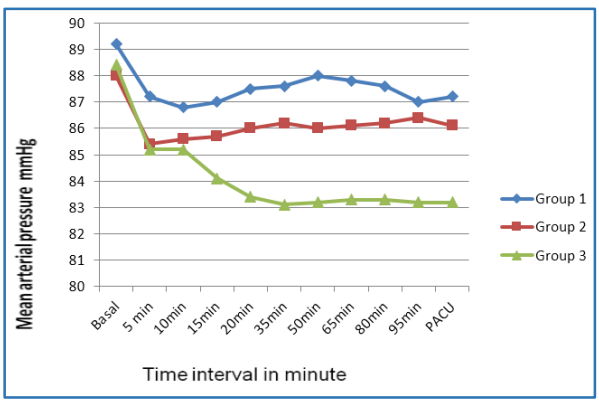

Figure 2. Showing Mean Arterial Pressure Difference in Three Groups (mmHg)

Haemodynamic parameters were stable in all the groups and there were no complications in any patient among the three groups. No statistically significant differences among the study groups in the number of patients who required Atropine, ephedrine and tramadol in 24 hours were seen (Table 3).

Variable	Group 1	Group 2	Group 3	P value
Patient Required Atropine (%)	2 (7%)	2 (7%)	3 (10%)	0.877
Patient Required Ephedrine (%)	2 (7%)	3 (10%)	3 (10%)	0.890
Patient Required Tramadol 1 mg/kg Intravenous in 24 hrs. (%)	18 (60%)	17 (57%)	16 (52%)	0.963
Hypotension (%)	5 (17%)	4 (12%)	4 (12%)	0.935
Sedation	0	0	0	0
Pruritus	0	0	0	0

Table 3. Number of Patients Required Atropine or Ephedrine Complications

Variables	Group 1	Group 2	Group 3	P value
1 hr.	0	0	0	0.0
6 hrs.	6	3	3	0.525
12 hrs.	6	5	3	0.644
18 hrs.	5	5	3	0.760
24 hrs.	5	4	2	0.561

Table 4. Showing Postoperative Visual Analogue Scale

Data presented as mode, h: hour, *P value <0.05 is statistically significant.

DISCUSSION

In our study, we have compared the addition of fentanyl (10 µg), buprenorphine (30 µg) and dexmedetomidine (5 µg) to 15 mg of 0.5% hyperbaric bupivacaine for spinal anaesthesia in patients undergoing hemiarthroplasty. Dexmedetomidine is an α_2 adrenoreceptor agonist. It has activity at a variety of location in the central nervous system. Sedative and anxiolytic effects are due to its action on locus coeruleus of brain stem. Dexmedetomidine is eight times more specific and highly selective α_2-adrenoreceptor agonists compared to clonidine. Stimulation of these receptors at dorsal horn neurons of the spinal cord reduces the sympathetic firing and also modulates the release of substance P and produces hyperpolarisation of dorsal horn neurons.[6],[15],[16],[17],[18]

Buprenorphine is an opioid and it act by partially stimulating kappa and mu opioid receptors and partially inhibiting delta opioid receptors and it has both spinal and supraspinal component of analgesia.[19] Buprenorphine effect to prolong the analgesic effect of local anaesthetic when added as adjuvant to spinal anaesthesia has been shown by recent studies.[20] Fentanyl is a narcotic analgesic with mu opioid receptor agonist activity when used intrathecally, it binds to opioid receptors in the dorsal horn and exhibit it's effects.[4]

In our study, patient's characteristics like age, sex, weight, duration of surgery was matched such that they will not influence the result of the study. There were no significant differences with respect to haemodynamic characters (heart rate, blood pressure) among the groups and also there were no significant side effects (sedation, hypotension, etc.) among the groups studied. Kanazi GE and his co-workers concluded that 3 µg dexmedetomidine when added to intrathecal bupivacaine resulted in rapid onset of motor block, prolongation in the duration of motor and sensory block with no haemodynamic derangement and sedation.[6] Similarly, it was shown that the addition of dexmedetomidine 3 µg to intrathecal 0.5% hyperbaric bupivacaine 6 mg in patients undergoing transurethral prostatectomy produced faster onset and a prolonged duration of sensory block and postoperative analgesia.[15] Similar to our results, a study by Vidhi Mahendru et al[1] showed that dexmedetomidine 5 µg with 12.5 mg bupivacaine leads to prolongation of motor and sensory block, preserved haemodynamics and decreased postoperative analgesic consumed compared to clonidine 30 µg, fentanyl 25 µg or 12.5 mg hyperbaric bupivacaine alone in patients undergoing lower limb surgery.

In this study, the addition of dexmedetomidine 5 µg to intrathecal 15 mg of 0.5% heavy bupivacaine was associated with significant prolongation of the time for the sensory spinal regression to S_1 level (P=0.006) when compared to other groups. Our study showed that motor regression to modified Bromage score 0 and time for request of first analgesia was significantly longer in dexmedetomidine group than other groups (P=0.0001). The results of our study are similar to the study results of the previous studies.[1],[4],[15]

CONCLUSION

Addition of dexmedetomidine (5 µg) to 15 mg of 0.5% heavy bupivacaine provided significantly longer duration of motor

and sensory nerve blockade and also the first request of analgesia in the postoperative period when compared with buprenorphine (30 µg) and fentanyl (10 µg) added to 15 mg of 0.5% heavy bupivacaine for hemiarthroplasty.

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