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DEXMEDETOMIDINE VERSUS FENTANYL AS AN ADJUVANT TO LOW DOSE INTRATHECAL BUPIVACAINE IN ELDERLY PATIENTS UNDERGOING LOWER LIMB ORTHOPAEDIC SURGERY

Dr Deepak Singh Associate Professor Dept of Anaesthesiology and Critical Care Pt. J N M Medical College, Raipur (C.G.)

Dr Rashmi Naik* Associate Professor Dept of Anaesthesiology and Critical Care Pt. J N M Medical College, Raipur (C.G.) *Corresponding Author

Dr Rashmi Thakur Associate Professor Dept of Anaesthesiology and Critical Care Pt. J N M Medical College, Raipur (C.G.)

Dr Chandrapal Bhagat Associate Professor Dept of Anaesthesiology and Critical Care Pt. J N M Medical College, Raipur (C.G.)

ABSTRACT

Introduction- Regional anaesthesia is the method of choice for most elderly patients undergoing elective lower limb orthopedic surgery since it results in reduced blood loss and transfusion needs, modification of the neuroendocrine stress response, producing less postoperative delirium and deep vein thrombosis. Subarachnoid block (SAB) is the most commonly used technique for these procedures as this is the low cost, quickest, most predictable and reliable method of regional anaesthesia. In this study, we aimed to compare the effect of low dose bupivacaine plus fentanyl, and bupivacaine plus dexmedetomidine in terms of characteristics of subarachnoid block, hemodynamic changes, postoperative analgesia and side effects in elderly patients undergoing lower limb orthopaedic surgery.

Method- The present cross sectional prospective hospital based study was conducted in the department of anaesthesia, pt J.N.M medical college Raipur (C.G.) India, during study period July 2017 to June 2018. Sixty ASA II and III, elderly patients scheduled to undergo elective lower limb orthopaedic surgeries were allocated into two groups to receive either bupivacaine plus fentanyl (group F) or bupivacaine plus dexmedetomidine (group D) intrathecally. The onset and duration of sensory and motor block, maximum sensory block level and time to achieve highest level of block, duration of analgesia, sedation scores, hemodynamic changes and side effects were recorded and statistically compared between two groups.

Results- The groups were comparable with respect to age, height, and weight, and ASA physical status.There was no significant difference between both the groups regarding onset time of sensory block and motor block. Group D had significantly longer duration of sensory block. Motor block was prolonged in group D as compared to group F. The mean duration of analgesia in Group D was 214±39.8 min while it was 369± 33.98 min in Group F, which was statistically significant (p=0.0001). There was no significant difference in hemodynamic parameters and side effects between both the groups.

Conclusion- Dexmedetomidine and fentanyl as adjuvant with low dose intrathecal bupivacaine provides satisfactory anesthesia and analgesia with haemodynamic stability in elderly patients undergoing lower limb orthopedic surgeries. However, the clinical advantage of dexmedetomidine over fentanyl is that, it prolongs duration of block and provides excellent quality of post-operative analgesia compared to fentanyl.

KEYWORDS : Dexmedetomidine, Fentanyl, Bupivacaine, Lower Limb Orthopaedic Surgery

INTRODUCTION

As life expectancy continues to increase, the number of older patients for orthopaedics surgery is steadily growing. Regional anaesthesia is the method of choice for most elderly patients undergoing elective lower limb orthopedic surgery since it results in reduced blood loss and transfusion needs, modification of the neuroendocrine stress response, producing less postoperative delirium and deep vein thrombosis.[1,2,3] Subarachnoid block (SAB) is the most commonly used technique for these procedures as this is the low cost, quickest, most predictable and reliable method of regional anaesthesia. However, the use of local anaesthetics in this technique is not without complications such as hypotension, bradycardia, neurological injuries and urinary retention etc.[2] Elderly patients are usually more vulnerable to these adverse effects, due to decline in organ function, change in the pharmacokinetics and pharmacodynamics of drugs and the presence of comorbidities.[1] Most of these complications are found to be dependent on the volume and dose of injected drug and the height of SAB.[4] To reduce the adverse hemodynamic effects associated with subarachnoid block in these patients, an appropriate adjuvant to low dose local anaesthetics can help to prolong the duration of spinal block and analgesia without compromising hemodynamic parameter.

Various adjuncts, such as opioids, α_2 adrenergic agonists (dexmedetomidine and clonidine), midazolam, neostigmine, ketamine, and magnesium sulfate are being used with local anaesthetics for prolongation of postoperative analgesia.[5] During the intrathecal or epidural administration, lipophilic opioids (fentanyl) has an early onset, shorter duration of action and fewer side effects than morphine, which has become one of the most commonly used neuraxial opioid.[7] Dexmedetomidine, a selective α_2 adrenergic receptor agonist ($\alpha 2/\alpha 1$ 1,600:1) has been shown to be a better adjuvant to intrathecal local anesthetics for analgesia.[8-10] Dexmedetomidine as an adjuvant has been extensively compared with fentanyl in spinal and epidural anaesthesia with conventional dose of bupivacaine in younger adults.[11,12] A variety of anatomical and physiological changes related to aging contribute to altered nerve block characteristics after subarachnoid administration of local anesthetics in elderly patients. With hyperbaric local anesthetic solutions, the maximal height of spinal analgesia achieved has been found to increase with age.[13] Lower doses of local anesthetics along with an adjuvant are preferred for spinal anesthesia in elderly patients.[5,13] Dexmedetomidine and fentanyl has been found to be effective for urological surgeries with low-dose bupivacaine.[14,15] The studies on these drug combinations with low dose intrathecal bupivacaine for lower limb orthopaedic surgery in elderly patient are relatively unexplored. So in our present study we compared the effect of addition of dexmedetomidine (5µg) or fentanyl (25µ g) to 8 mg hyperbaric bupivacaine 0.5% in lower limb orthopaedic surgery in elderly patients in terms of characteristics of spinal block, hemodynamic changes, postoperative analgesia and side effects.

MATERIALS AND METHODS

The present cross sectional prospective hospital based study was conducted in the department of anaesthesia, pt J.N.M medical college Raipur (C.G.) India, during study period July 2017 to June 2018. After Institutional Ethics Committee approval and informed consent, the present study was conducted in our institute in 60 patients of 60-75 yr of age, American Society of Anesthesiologists physical status (ASA) II

and III posted for lower limb orthopedic surgery. Patients were allocated into two groups, group F and D (n=30). Patients with contraindication to regional anaesthesia, allergy to study drugs, history of significant coexisting diseases like ischemic heart disease, hypertension, impaired renal functions, rheumatoid arthritis, and severe liver disease were excluded from the study. All patients were examined and investigated a day prior to surgery, and were familiarized with visual analogue scale (VAS) [16] and its use for measuring the postoperative pain. They were advised fasting for 6 h. Before commencing regional anesthesia, standard monitoring was established using ECG, noninvasive blood pressure, and SpO_2 and baseline parameters were recorded. Intravenous access was secured with 18G cannula and all patients were preloaded with ringer lactate 300 ml. Under all aseptic precautions subarachnoid block was performed in the sitting position at level of L_{2-3} or L_{3-4} vertebral level using 25-gauge Quincke spinal needle. Patients of group F received 1.6 ml (8 mg) 0.5% bupivacaine heavy with 25 µg fentanyl and group D received 1.6 ml (8 mg) 0.5% bupivacaine heavy with 5 µg dexmedetomidine. The required dose of dexmedetomidine was drawn using a 40 unit insulin syringe (2 units of 100 mcg/mL preservative-free dexmedetomidine loaded in a 40 unit insulin syringe). Injections were given over approximately 10 to 15 seconds. The completion of injection was taken as the time zero for induction of anesthesia.

The onset and duration of sensory and motor block, highest level of sensory block, time to regression to S1dermatome, and duration of analgesia were recorded. The onset of sensory block was defined as the time between injection of intrathecal anaesthetic and the absence of pain at the T10 dermatome as evaluated by pinprick at midclavicular line anteriorly every 2 min for 20 min after the injection, thereafter every 15 min. The maximum level of sensory block was considered when the loss of sensation was recorded at the same dermatomal level for 2 consecutive time intervals. The highest sensory level and time to achieve was noted. Duration of sensory block was measured as the time taken for the sensory block to regress up to S1 dermatome.

The motor block was assessed according to modified Bromage score.[17] Heart rate and mean blood pressure pressure was recorded at 5min before regional anesthesia and at 5, 10, 15, 30, 45 and 60 min after anaesthesia. Hypotension was defined as systolic BP <90 mmHg or fall in mean arterial pressure more than 30% from baseline and was treated with injection mephentermine 6 mg boluses. Bradycardia was defined as fall in HR below 50 beats/min and treated with injection atropine 0.6 mg.

In the post-anesthetic care unit (PACU) sensory block regression (sensory regression to S1 level) and motor block recovery (modified Bromage score of zero) were assessed every 15 min after completion of surgery along with the vital signs.

Postoperatively, the pain score was recorded using visual analogue pain scale (VAS 0 to 10, 0: no pain; and 10: the worst imaginable pain), initially every hours for 2 h, then at every 2 h for the next 8 h and thereafter every 4 h till 24 h. Patients were allowed to receive rescue analgesics (dose of IV tramadol 50 mg) on demand or on VAS > 4. Duration of analgesia was measured as time from injection of the drug given in subarachnoid space to the patient's first request for rescue analgesic. Ramsay Sedation Score [18] was used to assess sedation postoperatively in patients. The incidence of adverse effects, such as nausea, vomiting, shivering, pruritus, respiratory depression, sedation, bradycardia and hypotension were recorded.

STATISTICALANALYSIS

Data was collected and analysed with the help of excel and graph-pad in stat software for statistical analysis. Proportion as number and percentage was determined for categorical variables like gender. Mean and standard deviation were determined for continuous variables. Student *t*-test was applied for comparison for continuous variables. The differences seen were evaluated for significance, *p* value less than 0.05 was taken as significant.

RESULTS

The groups were comparable with respect to age, height, and weight, and ASA physical status. There was no significant difference in the type and duration of surgery. The numbers of patients under each type of surgery performed on the lower limb were similar amongst the groups thereby keeping the comparison unbiased **[Table 1, 2].**

TABLE 1: DEMOGRAPHIC PROFILE

Variable	Group F	Group D	p-value
Age (years)*	68.8±6.3	69.6±6.2	0.6220
Sex (M:F)	21:9	19:11	0.487
Height (cm)*	165.5±5.2	167.0±6.9	0.3456
Weight (kg)*	66.0±7.7	68.7±10.2	0.2520
ASA II:III	23:7	20:10	0.677
Duration of surgery (minutes)*	100 ±33.27	96.11±31.42	0.6432

*Values are expressed as Mean ± SD

TABLE 2: TYPE OF SURGERY

Type of surgeries	Group F	Group D
Dynamic hip screw fixation	14	16
Shaft of femur ORIF	11	9
Tibia ORIF	5	5

The groups were comparable with respect to age, height, and weight, and ASA physical status. There was no significant difference in the type and duration of surgery. The numbers of patients under each type of surgery performed on the lower limb were similar amongst the groups thereby keeping the comparison unbiased **[Table 1, 2]**.

TABLE 3: CHARACTERISTICS OF SUBARACHNOID BLOCK

Characteristics of subarachnoid block	Group F	Group D	
Time of onset of sensory block[min]	4.9± 1.9	4.3± 1.67	0.1990
Time of onset of motor block[min]	8.85±2.67	8.25± 2.45	0.3682
Time to reach maximum sensory level [min]	11.90± 1.7	10.9± 2.1	0.0472
Time for sensory regression to S1 from highest sensory level (min)	159± 36.10	292± 36.10	0.0001
Duration of motor block[min]	167.0±24.8	258±39.1	0.0001
Duration of analgesia[min]	214±39.8	369± 33.98	0.0001
Mean sedation score	1.02 ± 0.2	1.18 ± 0.9	0.3458

Values are expressed as Mean ± SD

TABLE 4: HIGHEST DERMATOME LEVEL OF SENSORY BLOCK

Level of sensory block	Group F *(n=30)*	Group D *(n=30)*
T6	0	0
T7	14(46.66)	17(56.66)
T8	15(50)	13(43.33)
T9	1(3.3)	0(0)

There was no statistically significant difference between two groups with respect to onset and time to reach peak of sensory block ($p > 0.05$). The mean time for S1 segment sensory regression was 292± 36.10 min in Group D and 159± 36.10 min in Group F ($p = 0.0001$) which was highly significant. There was no statistically significant difference between two groups in time to onset of motor block ($p > 0.05$). The duration of motor block was 258±39.1 min in group D and 167.0±29.8 min in Group F ($p=0.0001$) which was statistically significant. The regression of motor block to Bromage 0 was significantly slower with the addition of dexmedetomidine. The highest level of block achieved in the two groups were same ie. T 7. **[Table 3,4].**

TABLE 5: MEAN HEART RATE (BPM)

Time interval	Group F	p value	Group D	p value	p value F vs D
Baseline	88.46±14.42		85.10±12.58		0.3402
After induction	92.83±16.03	0.2715	89.5±12.56	0.1805	0.3742
5 min	90.46±17.17	0.6270	89.53±15.29	0.2254	0.8254
10 min	87.06±14.13	0.7055	85.80±16.94	0.8564	0.7555
15 min	85.13±13.41	0.3582	83.93±14.72	0.7419	0.7425
30 min	83.1±11.44	0.1162	81.80±11.64	0.2960	0.6643
45 min	83.36±11.37	0.1337	81.63±11.52	0.2698	0.5605
60 min	82.9±10.95	0.0980	80.73±11.64	0.1679	0.4600

TABLE 6: MEAN BLOOD PRESSURE (MMHG)

Time interval	Group F	p value	Group D	p value	p value F vs D
Baseline	76.26±7.23		75.80±7.42		0.8087
After induction	78.26±6.8	0.2743	77.00±7.24	0.5286	0.4899
5 min	76.16±6.20	0.9543	73.46±9.34	0.2871	0.1923
10 min	73.93±6.63	0.1984	73.2±7.84	0.1923	0.6984
15 min	72.93±7.05	0.0761	73.03±9.34	0.2085	0.9628
30 min	72.80±6.17	0.0509	73.1±7.61	0.1694	0.8674
45 min	73±5.64	0.0563	73.2±7.22	0.1743	0.9052
60 min	73.13±5.94	0.0721	73.13±6.61	0.1465	1.0000

TABLE 7: SIDE EFFECTS

Side Effects	Group F	Group D	p Value
Nausea	1	0	0.3176
Vomiting	0	0	-
Shivering	1	0	0.3176
Pruritus	0	0	-
Respiratory depression	0	0	-
Hypotension	0	0	-
Bradycardia	1	1	1.000

The mean duration of analgesia and time to rescue analgesic were significantly longer in group D as compared to group F. The patients in both the groups were hemodynamically stable intraoperatively and postoperatively. There was no significant difference in heart rate and mean blood pressure in both groups. One patient in group D and one patient in group F had bradycardia but it was managed successfully with atropine 0.6 mg IV. Patients in both groups did not show statistically significant difference in the incidence of side One patient in fentanyl group experienced nausea and one patient in group F had shivering. The mean sedation score was 1.18 ± 0.9 in Group D as compared to 1.02 ± 0.2 in Group F, which was statistically insignificant (p =0.3458*)*. **[Table -5,6,7]**

DISCUSSION

Our study compared dexmedetomidine and fentanyl as adjunct for low-dose intrathecal bupivacaine 8mg for elderly patients undergoing lower limb orthopaedic surgery. The results of our study showed that addition of 5 µg dexmedetomidine with low-dose intrathecal bupivacaine effectively prolonged both sensory and motor block along with excellent quality of analgesia as compared to 25 µg fentanyl. Our results are consistent with previous author's findings. [11,12,19] However, we employed low dose of bupivacaine (8mg) as compared to previous ones (10mg-15mg). The exact mechanism by which dexmedetomidine prolongs the motor and sensory block of local anesthetics is not well known. It could be due to synergistic effect secondary to the different mechanisms of action of the local anesthetics and intrathecal alpha2 adrenoreceptor agonists. Local anesthetics act by blocking sodium channels. Alpha2 adrenoreceptor agonists act by binding to the presynaptic C-fibers and post-synaptic dorsal horn neurons. [20, 21, 22] It prolongs sensory block by the depressing release of C-fiber transmitters and by hyperpolarization of post-synaptic dorsal horn neurons. It prolongs motor block by binding of alpha2 adrenoreceptor agonists to the motor neurons in the dorsal horn. [11,20,22]

We found that the onset of sensory block was statistically comparable in both dexmedetomidine and fentanyl groups. El-Attar et al, and Safari et al, in their studies observed that onset of sensory block was faster in dexmedetomidine group as compared with fentanyl when given intrathecally along with bupivacaine.[24,25] Similar to our results Mahendru *et al* and Gupta R *et al* concluded that both had no significant difference in the onset of sensory blockade.[19,23] The onset time observed in the above studies were relatively longer than our study. Longer duration of onset may be because of the use of different criteria for the sensory onset. Onset of block in Mahendru et al study was time taken to achieve T8 level whereas in R Gupta *et al study* it was time taken to achieve highest sensory level. However, in our study it was the time taken to achieve T10 level of sensory block. Similarly onset of motor block in both the groups was comparable which was similar with the findings of previous investigators.[11,19,23] Safari et al[24] and Ravipati reported faster onset of motor block for dexmedetomidine as compared to fentanyl.[26] The difference in results observed by different authors regarding time to onset of motor block may be due to different study population, dose, volumes, concentration and baricity of local anesthetic solutions used.

The maximal sensory block height achieved was T7 dermatome in both the groups. In a study conducted by Mahendru *et al* maximal block height achieved was T6 in both fentanyl and dexmedetomidine group.[19] In another study, it was found that the maximum height of sensory block achieved was T5 with dexmedetomidine and T6 with fentanyl as adjuvant to local anesthetic.[23] We used low dose 8 mg of bupivacaine, which could justify a lower level of blocks in our study.

Our study revealed that intrathecal dexmedetomidine (5 µg) as an adjuvant with intrathecal hyperbaric bupivacaine significantly prolongs both sensory and motor block compared with intrathecal fentanyl (25 µg). Mean duration of sensory block and motor block was prolonged in group D as compared to group F. Similar results were observed by Mahendru *et al* who compared intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery and found that 5 μg dexmedetomidine produced more prolonged motor and sensory block as compared to 25 µg fentanyl. [19] Similarly Al-Ghanem *et al* had studied the effect of addition of 5 μg dexmedetomidine or 25 μg fentanyl intrathecally to 10 mg isobaric bupivacaine in gynaecological surgery and concluded that 5 μg dexmedetomidine produces more prolonged motor and sensory block as compared to 25 µg fentanyl.[11] Similar result also noted by El-Attar et al, and Safari et al., who compared intrathecal dexmedetomidine with fentanyl as adjuvant to bupivacaine.[24,25] But the total duration of sensory and motor block in the above study are different from our study. It may be due to the same reason given above. Nevertheless, above mentioned authors found that adding dexmedetomidine and fentanyl as adjuvant to intrathecal bupivacaine was associated with prolongation of sensory and motor block. We noted the mean duration of analgesia was also significantly longer in Group D ($p< 0.0001$). Similarly, significantly improved analgesic efficacy was seen by other authors on comparison of dexmedetomidine and fentanyl as intrathecal adjuvant. [11,19,23,24,25]

Moreover, Eid HE et al and Hala EA et al observed dose dependent reduced analgesic requirement with increasing dosages of intrathecal dexmedetomidine (5,10,and15µg). [27,28] One of disadvantage of spinal anaesthesia is bradycardia and hypotension, especially in elderly. In the current study, these side effects were not significant, probably because we used low dose of local anesthetics along with low dose of dexmedetomidine and fentanyl. Mahendru *et al*[19] and Gupta R *et al*[23] *noted similar result with higher dose of* bupivacaine. Small dosages of adjuvants may also be responsible for minimal sedation noted in both the groups in our study. Gupta et al, observed significantly higher sedation with 10 μg dexmedetomidine as compared to 2.5 μg and 5 μg dexmedetomidine. [29]

In our study no significant incidence of adverse effects were observed in either group. Similar results were found in previous studies. [19,23,24,]

CONCLUSION

Dexmedetomidine and fentanyl as an adjuvant with low dose intrathecal bupivacaine (8mg) provide satisfactory anesthesia and analgesia with haemodynamic stability in elderly patients undergoing lower limb orthopedic surgeries. However, the clinical advantage of dexmedetomidine over fentanyl is that it prolongs duration of block and provides excellent post-operative analgesia as compared to fentanyl.

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