A comparison of fentanyl, dexmedetomidine and combination of fentanyl with dexmedetomidine on the quality of subarachnoid block and postoperative analgesia: A double-blind controlled study

INTRODUCTION

Many adjuvants have been used with local anaesthetics in spinal anaesthesia to abstain from intraoperative pain and provide prolonged postoperative analgesia. Dexmedetomidine, the highly selective α2-agonist drug, is used as a neuraxial adjuvant along with fentanyl.

Spinal anaesthesia is the most commonly used regional anaesthetic technique for infra umbilical surgeries. However, postoperative pain control is a major concern because of the shorter duration of action of local anaesthetics used in spinal anaesthesia; thus, early analgesic intervention is needed in the postoperative period. Several adjuvants, such as clonidine, dexmedetomidine and opioids, have been studied to prolong the effect of spinal anaesthesia. Dexmedetomidine and fentanyl alone are commonly used and well-accepted adjuncts for subarachnoid block in patients scheduled for lower limb surgeries.

The present study was designed to compare the efficacy and postoperative analgesia as the primary objective and haemodynamic stability as a secondary objective with a combination of fentanyl and dexmedetomidine.

METHODS

After obtaining Institutional Ethical Committee approval, this prospective randomised double-blinded study was carried out on ninety patients of both genders, aged between 18 and 60 years, belonging to the American Society of Anesthesiologists (ASA) physical status grade I and II undergoing elective infra umbilical surgeries under spinal anaesthesia. Exclusion criteria were patient with history of allergy to the study drugs, ischaemic heart disease, atrioventricular block, incomplete or partial heart blocks, chronic alcoholics, intake of alpha-blockers, coagulopathy, pregnancy and any contraindication for spinal anaesthesia.

All patients were shown the Visual Analogue Scale (VAS) and were apprised about the same during the pre-operative visit one day prior to the surgery and were familiarised with the measurement of postoperative pain. All the patients were kept for 6 h fasting prior to surgery and received alprazolam 0.5 mg as premedication the night before the day of the surgery.

The patients were randomly divided into three groups of 30 patients each (Group F, Group D and Group DF) by an independent anaesthesiologist as per computer-generated random numbers. The senior resident, who had not participated in the study, prepared the drug. The attending anaesthesiologist was blinded to the drug, and observed and recorded the parameters.

On arrival at the operating room, preloading was completed with Lactated Ringer’s solution (10 mL/kg body weight). Standard monitoring, including electrocardiogram (ECG), automated noninvasive blood pressure (NIBP), heart rate (HR), respiratory rate (RR) and pulse oximetry was performed.

Group F: received 2 ml (10 mg) of 0.5% hyperbaric bupivacaine with 0.5 ml (25 µg) fentanyl plus 0.5 ml normal saline,

Group D: received 2 ml (10 mg) of 0.5% hyperbaric bupivacaine with 0.5 ml (5 µg) dexmedetomidine plus 0.5 ml normal saline

Group DF: received 2 ml (10 mg) of 0.5% hyperbaric bupivacaine with 0.5 ml (5 µg) dexmedetomidine in normal saline and 0.5 ml (25 µg) fentanyl.

The total volume of solution in all the groups was 3 ml. The subarachnoid block was administered at the L2–3 vertebral level using a 25-gauge Quincke spinal needle in the sitting position. The time of injection (zero time), was noted and patients were positioned in the supine position.

The onset of sensory block and motor block, duration of sensory block and motor block, time of first rescue analgesia, total analgesic requirement and haemodynamics were recorded. The onset of sensory block was defined as the time between the intrathecal
injection of anaesthetic (zero time) and the absence of pain at the T8 dermatome, which was assessed by a sterile pinprick. The duration of sensory block was defined as the time of regression to the S2 level from the maximum block height, evaluated by a pinprick. The motor level was assessed according to the modified Bromage score.[3] Time for motor block onset was defined as time to achieve the modified Bromage score of 1. The modified Bromage score 6 was assumed as complete motor block recovery. All parameters such as the onset of sensory and motor block, regression of sensory and motor block, and time of first rescue analgesic were measured from zero time. Surgery was permitted to begin on achieving adequate sensory block height (T8). Vitals were recorded 5 min prior to intrathecal injection, at 5, 10, 15, 20 and 25 min after and subsequently at every 15 min interval. VAS was assessed in the postoperative period every 15 min.

In the post-anaesthetic care unit (PACU), after completion of surgery till the time of regression of two segments from the maximum level of block, motor block recovery (modified Bromage score of six) and sensory block regression was assessed every 15 min along with the vital signs and VAS scores. The time of first rescue analgesic was defined as the time from injection of a spinal drug (zero time) to the time when the patient complains of pain with a VAS score of ≥3. Any patient showing VAS ≥3 was administered a supplemental dose of IV tramadol 1 mg/kg. The total amount of analgesic required by the patients in the next 6 h postoperatively was recorded in all the groups.

Statistical analysis was done by the Statistical Package for the Social Sciences version 22 (SPSS V22) International Business Machines, New York, USA. Continuous variables are presented as mean ± standard deviation (±SD), and categorical variables are presented as absolute numbers. Data were entered in MS-Excel and analysed. Analysis of variance (ANOVA) test, and Chi-square/Fisher Exact tests were applied to find significance. P < 0.05 was considered statistically significant.

RESULTS

All patients (n = 90) completed the study, and there was no statistical difference in patients’ demographics and duration of surgery [Table 1]. The mean time of onset of sensory and motor block was quicker in Group F (7.24 ± 0.85 and 8.0 ± 0.85) as compared to Group D (7.97 ± 1.01 and 9.28 ± 1.01) and Group DF (7.67 ± 0.98 and 9.16 ± 0.82). It was statistically significant (P < 0.05). The mean time for regression of sensory and motor nerve block was significantly longer in Group D and Group DF compared to Group F (P < 0.001). The mean time of the first rescue analgesic was also statistically longer in GroupDF(471.53 ± 30.94)andGroupD(387.17 ± 18.30)as compared to Group F (191.73 ± 15.00) (P < 0.001). The total amount of rescue analgesic used by participants of Group F (113.77 ± 11.71) was significantly more as compared to Group D (61.1 ± 8.44) and Group DF (64.97 ± 7.65) (P < 0.001) [Table 2].

In our study, the mean HR from 5 min to 240 min was stable in Group F and Group D in comparison to Group DF and was statistically significant [Figure 1].

The mean systolic blood pressure in Group DF was lower than those in Group D and Group F from the...
3rd min to the 15th min and was statistically significant. The mean systolic blood pressure of participants in Group D was lower than those in Group F and Group DF from the 30th minute to 240 minutes and was statistically significant [Figure 1].

The mean diastolic blood pressure of participants in Group DF was lower than those in Group D and Group F from the 5th min to the 10th min and was statistically significant. The mean diastolic blood pressure of participants in Group D was lower than those in Group F and Group DF from the 15th min to the 120th min and was statistically significant [Figure 1].

**DISCUSSION**

Few trials comparing fentanyl, dexmedetomidine and a combination of the two as adjuvants to intrathecal bupivacaine have been published. The present study demonstrates that adding intrathecal dexmedetomidine 5 µg to bupivacaine-fentanyl mixture (DF group) for infra-umbilical surgeries provided significantly prolonged postoperative analgesia for first rescue analgesic request as compared with D and F groups (P < 0.001). Although previous studies have demonstrated similar results of prolonged postoperative analgesia when they added 5 µg dexmedetomidine or 25 µg fentanyl, our study using a combination of dexmedetomidine with fentanyl has demonstrated a much more prolonged duration of first rescue analgesic probably owing to the synergistic effect offered by the combination of dexmedetomidine with fentanyl. The mean VAS score was low in all the groups. The mean total consumption of IV tramadol in the first 6 h postoperatively was significantly higher in the F group compared to the D and DF groups. But there was no difference between D and DF groups similar to the study carried out by Mohamed et al. Local anaesthetics act by blocking sodium channels; however, α2 adrenoceptor agonists act by binding to the presynaptic C-fibres and postsynaptic dorsal horn neurons. They produce analgesia by depressing the release of C-fibre transmitters and by hyperpolarisation of postsynaptic dorsal horn neurons. The complementary action of local anaesthetics and α2 adrenoceptor agonists accounts for their profound analgesic properties. The prolongation of the motor block of spinal anaesthetics may be the result of the binding of α2 adrenoceptor agonists to the motor neurons in the dorsal horn. Intrathecal fentanyl exerts its effects by combining with opioid receptors in the dorsal horn of the spinal cord and may have a supraspinal spread and action. Intrathecal fentanyl, when added to spinal local anaesthetics reduces visceral and somatic pain.

The time of sensory and motor block was significantly shorter in the F group compared to the D or DF groups. These findings contrast with the previous studies where there was no difference between the fentanyl and dexmedetomidine groups.

The duration of sensory block was markedly prolonged for the D and DF groups with respect to the F group which could be attributed to a higher intrathecal volume of drugs (3 ml) similar to Mahendru et al.

The duration of motor block in the DF and D groups was significantly prolonged, similar to previous studies. Dexmedetomidine has been studied as an epidural adjunct by various authors who have observed its synergism with local anaesthetics. It is observed to prolong the motor and sensory block duration time and postoperative analgesia without any additional morbidity.

We observed that changes in SBP, DBP and HR in the D and DF groups were higher than the F group. The highest decline occurred between 5 min and 15 min after spinal injection and was rather stable later. Unlike our findings, other studies did not report any significant difference between fentanyl and dexmedetomidine regarding haemodynamic status.
In our study, we noted hypotension in three patients in each F and D groups and two patients in the DF group. Hypotension was treated with an incremental dose of injection ephedrine.

Bradycardia episodes were noted in four patients in the D group, one patient in the F group and two patients in the DF group, which were statistically not significant and were treated with injection atropine 0.6 mg IV stat.

**CONCLUSION**

We conclude that intrathecal dexmedetomidine with fentanyl as an adjuvant to bupivacaine is a much better alternative to fentanyl and dexmedetomidine for long duration of surgical procedures due to its prolonged analgesic properties and motor blockade. The combination of dexmedetomidine with fentanyl also resulted in less postoperative rescue analgesic requirement.

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**Conflicts of interest**

There are no conflicts of interest.

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