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Research Article

A Comparative Study of the Efficacy of Intrathecal Injection of Hyperbaric Bupivacaine with Fentanyl Versus Hyperbaric Bupivacaine with Dexmedetomidine in Lower Abdominal Surgeries: A Prospective Randomized Study

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ABSTRACT

Background: Spinal anaesthesia is the most common technique used for lower abdominal surgeries. Spinal anaesthesia using plain hyperbaric bupivacaine has disadvantages like delayed onset, shorter duration etc. Adding adjuvants like fentanyl, dexmedetomidine has overcome these disadvantages and improve post operative analgesia and stable hemodynamic condition with minimal side effects. Aim of the study was to determine the time of onset and duration of sensory and motor block, sedation score and postoperative analgesic efficacy of Fentanyl and Dexmedetomidine as adjuvant to bupivacaine in lower abdominal surgeries.

Methods: This prospective, double blind, randomized study included total 100 patient-divided equally in 2 groups (group F-fentanyl and group D-dexmedetomidine) after matching the inclusion and exclusion criteria. Group F received 3ml of 0.5 % injection Hyperbaric Bupivacaine + 25 mcg Fentanyl and Group D received 3ml of 0.5 % injection Hyperbaric Bupivacaine + 5mcg Dexmedetomidine intrathecally. The onset and duration of sensory and motor block, sedation score, duration of postoperative analgesia and need of rescue analgesia along with haemodynamic parameters were recorded.

Results: The mean time for onset of sensory block in group D was (3.5 ± 0.88 mins) significantly lower than group F (4.4 ± 1.2 mins) (p=0.001). And the mean time of onset of motor block in group D (3.23 ± 1.0mins) was significantly lower than in group F (4.3 ± 1.1 mins). Duration of sensory and motor block was significantly higher in group D as compared to group F. The mean analgesic dose in group D was 1.4 ± 0.78 and in group F was 3.6 ± 0.73(p<0.005).

Conclusion: From our study we concluded that Dexmedetomidine is a better adjuvant than Fentanyl as it provides rapid onset and prolonged sensory and motor block, hemodynamic stability with excellent post operative analgesia.

Introduction

Most preferred mode of anaesthesia for lower abdominal surgeries is spinal anaesthesia. It is easy, economical, simple to perform and produces effective and longer duration of anaesthesia with complete motor relaxation and less postoperative pulmonary, thromboembolic, surgical, and metabolic stress complications [1].

Single drug spinal anaesthesia e.g., plain hyperbaric bupivacaine is most used local anaesthetic agent acts by

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blocking voltage gated sodium channel on neuronal membrane and produces sensory and motor block. It has disadvantages like shorter duration, less postoperative analgesia, intraoperative visceral pain, and nausea-vomiting. To overcome this, various adjuvants have been added to shorten the onset of block, prolong the duration of block and effective postoperative analgesia [2-3]. Frequently used adjuvants are adrenaline, tramadol, fentanyl, clonidine, magnesium sulphate.

Fentanyl is synthetic opioid acts on mu receptor as agonist to produce analgesia. It uses as adjuvant to local anaesthetic in spinal anaesthesia to provide longer duration of sensory and motor block and good quality of perioperative analgesia. But it has side effects like pruritus, delayed respiratory depression, muscle rigidity and constipation [4].

Dexmedetomidine hydrochloride is newer highly selective alpha-2 agonist and used as sedative, analgesic, and anxiolytic. It modifies nociceptive neurotransmission and terminate pain signals. It inhibits release of noradrenaline and provides hypnotic and supraspinal analgesic effect. When added as adjuvant to local anaesthetic, it significantly prolongs the duration of sensory and motor block and post operative analgesia and stable hemodynamic condition with minimal side effects like hypotension, bradycardia [5].

Therefore, this study was performed to determine the primary objectives such as onset and duration of sensory and motor blockade, sedation score, duration of postoperative analgesic efficacy of Fentanyl and Dexmedetomidine as adjuvants to bupivacaine in subarachnoid block during lower abdominal surgeries. Secondary objectives were intraoperative hemodynamic changes in heart rate, blood pressure and respiratory rate, oxygen saturation and adverse effects if any.

Methods

This prospective, double blind, randomized study was conducted at GMERS medical college, Gandhinagar, Gujarat, India Registration No.: ECR/535/Inst/GJ/2014/RR-20; Office of Drug Controller General, India).

Registration with NECRBHR: EC/NEW/INST/2021/2224, Dept. of Health Research, India) from November 2019 to October 2020 after getting approval from institutional ethical committee and patient's informed and written consent and for determining the sample size, probability sampling technique was used and sample size was counted based on:

Confidence interval (2 sided) -95%
Power -80%
Ratio of sample size (Group F/Group D)- 1

These details were entered in open-sourced statistical website-open Epi for calculation (Table 1) and sample size of 100 patient were divided in 2 groups. Group F-fentanyl group and group D-dexmedetomidine contains 50 participants in each group. Study sample included all the patients of age 18-65 years, ASA grade I&II, wt.-30-80kg, having height of 150-190cms posted for elective lower abdominal surgeries and exclusion criteria included patient refusal, ASA grade 3/4, any allergy or contraindication to local anaesthetic drug, fentanyl or dexmedetomidine. Patients were randomly allocated by coin toss method in one of the following groups: Group F(n=50) and Group D(n=50).

Drug preparation and data collection was done by another anaesthesiologist who was unaware of group allocation and drugs used in study. Volume of drug was made equal 3.5 ml for both the groups by diluting 1 ml Dexmedetomidine with NS in 10 ml syringe (10 µg/ml) and taking 0.5 ml(5microgram) +3ml 0.5% Hyperbaric Bupivacaine for group D and 0.5 ml Fentanyl (25 µg) + 3 ml 0.5% Hyperbaric Bupivacaine for group F.

Table 1- Probability sampling technique was used for considering the patient in flow rate in this hospital during fixed study period

	Group F	Group D	Difference
Mean of VAS [(6)] score	7.24	6.8	0.44
Standard deviation	0.99	0.5	
Variance	0.98	0.25	

Procedure and assessment

Pre-anaesthetic checkup was carried out a day before surgery with detailed history, general and systemic physical examination, and routine investigations. All patients were informed about study procedure along with advantages and disadvantages. Informed, written consent for patient participation & spinal anaesthesia was obtained. Patient was kept NIL BY MOUTH for 8hrs. Preparation of Operating Theatre, anaesthesia machine, all equipments, spinal anaesthesia tray and emergency drugs were kept ready. After arrival of patient in preoperative room, IV line was secured using 18 G IV cannula and premedication (Inj. ondansetron 0.1mg/kg & inj. pantoprazole 0.8mg/kg) was given. Preloading was started with 15ml/kg with Ringer lactate 15 to 20 mins before surgery. Patients were randomly allocated (coin toss method) into two groups, Group D (Dexmedetomidine) and group F (Fentanyl). In operation theatre, all standard monitors such as NIBP, pulse oximeter, ECG were attached & baseline vitals were recorded. Under all aseptic precautions, spinal anaesthesia was performed at L3 – L4 intervertebral space through a midline approach in sitting position using 25 G quinck's spinal needle. After confirming free flow of cerebrospinal fluid, the following drug was given according to group of patients. Then patient returned to supine position. Group F received 3ml of 0.5 % injection Hyperbaric Bupivacaine + 25 mcg Fentanyl intrathecally.

Group D received 3ml of 0.5 % injection Hyperbaric Bupivacaine + 5mcg Dexmedetomidine intrathecally.

Sensory block was assessed by pin prick method, every 2 min after subarachnoid block for 10min, then every 5min for next 20 min, and then every 30min for next 2 hours. Recorded parameters were -onset- from injection to T10 level (in min), highest sensory level and time to reach that level, time from injection to regression to S1 level (min).

Motor block was assessed based on modified bromage scale at same duration as sensory block –Recorded Parameters-onset- from injection to bromage 1(min), reaching maximum bromage 3 level(min) and regression from injection to bromage 0 (min), Sedation score was recorded based on Modified Ramsay sedation scale [6] used every 30mins till 180mins. Duration of postoperative analgesia was recorded by Visual analogue scale and counted as from spinal injection to need of 1st dose of rescue analgesia. Supplemental analgesia with inj.diclofenac was given when VAS>4. Secondary outcomes recorded every 2min for 10min, then for every 10min for next 50min and then every 15min till 90min.

Data analysis and confidentiality

Collected data was entered in the Microsoft excel data sheet and data analysis was done with the help of Epi. Info7.2 software. All the information collected was strictly used for study purpose and confidentiality was strictly maintained.

Results

Total 100 participants were included in this study equally divided in 2 groups -group F and group D. Demographic data like age, sex, weight, height, and ASA status in both study groups were comparable and there was no statistically significance (Table 2).

Table 2- Demographic profile of both the groups (mean +/- SD)

Variables	Group F (=50)	Group D (=50)
Age (in years)	43.6± 13.3	45.4 ± 12.4
Sex(M/F)	33/17	30/20
Weight (kg)	62.1 ± 7.3	62.4 ± 7.6
Height (cm)	160.0 ±4.96	160.3 ± 4.7
ASA grade I/II	21/29	24/26

Primary outcomes:

The mean time of onset of sensory block was significantly lower in group D (3.5 ± 0.88 mins) as compared to group F (4.4 ± 1.2 mins) (Figure 1). Mean time of onset of motor block in group D (3.23 ± 1.0 mins) was significantly lower than in group F (4.3 ± 1.1 mins) (Figure 1). The mean time for maximum sensory block was significantly lower in group D (9.4± 1.6 mins) as compared to group F (11.0 ± 2.5 mins) (Figure 2). Mean time for maximum motor block in group D (8.3 ± 1.7 mins) was significantly lower than in group F (9.3 ± 2.1 mins) (Figure 2). The duration of sensory analgesia was significantly higher in group D (328.6 ± 66.5 mins) as compared to group F (174.2 ± 21.9 mins) (Figure 3). Duration of motor block in group D (295.7 ± 63.0 mins) was significantly higher than in group F (143.8 ± 19.2 mins (Figure 3). The mean sedation score was significantly higher in group D at 60 minutes (2.24 ± 0.47), 90 minutes (2.38±0.53) and at 120 minutes (2.18±0.38) intra-operatively as compared to patients in group F which was at 60 minutes (2.02 ± 0.14), 90 minutes (2.04 ± 0.19) and at 120 minutes (2.0 ± 0). This observed difference was found to be statistically significant. It was found that out of 50 patients 27 patients in group D requested for rescue analgesia only one time, 14 patients in group D and 2 patients in group F requested for 2nd analgesic dose, 5 patients in group D and 23 patients in group F requested for 3rd analgesic dose, 20 patients and 5 patients requested 4th and 5th dose of analgesic dose respectively. 4 patients in group D did not request for any analgesic dose. From observation we found the mean analgesic dose in group D is 1.4 ± 0.78 and in group F is 3.6 ± 0.73. It has been observed that requirement of inj diclofenac sodium dose in first 24 hrs. post operatively was significantly lower in group D as compared to group F ($p<0.005$). The mean post-operative visual analog score was significantly lower in group D at 6hrs (1.8 ±1.1), 12hrs (3.3 ± 0.9), 18hrs (3.3 ± 0.9) and 24hrs (3.3 ± 0.9) ($p=0.001$) as compared to patients in group F (Figure 4).

Secondary outcome: hemodynamic parameters

The mean basal heart rate in group D was (88.5±8.9) bpm and group F was (90.0± 9.4) bpm, which was comparable in both groups. After intrathecal injection, at 2 min, 4 min, 6 min and 8 min, 20 mins fall in the heart rate was statistically significant in group D as compared to group F, after 30 mins it remained stable and comparable in both the study groups. There was no statistically significant difference with respect to heart rate. The mean SBP in group D was 130.5 ±12.8mmHg and group F was 131.6±10.3 mmHg, which was comparable in both groups. After intrathecal injection, mean SBP was decreased in both groups during intraoperative period (2 mins to 90 mins) which was significant in group D compared with group F. Except at 20 mins and 40 mins which was significant. The mean DBP in group D was (79.8±9.1) mmHg and in group F was (82.1±7.8) mmHg, which was comparable in both groups. After intrathecal injection, both groups showed fall in DBP from 2 mins to 40 mins and was comparable in both groups with no statistically significant difference. At 50 minutes, 60 mins and 75 mins, the DBP fall was significantly in group D as compared to group F. At 90 mins the mean DBP was stable comparable between both groups. No statistically significant difference between these two groups were noted. The mean MAP in group D was (96.7± 9.7) mmHg and group F was (100.3± 7.6) mmHg, which was comparable in both groups. After intrathecal injection, both groups showed fall in MAP

initially from 2 mins to 40 mins and this fall was comparable in both groups, no statistically significant difference between two groups. At 50 minutes, 60 mins and 75 mins the MAP was fall significantly in group D as compared to group F. At 90 mins the mean MAP was stable and comparable between two groups. No statistically significant difference between these two group with respect to MAP.

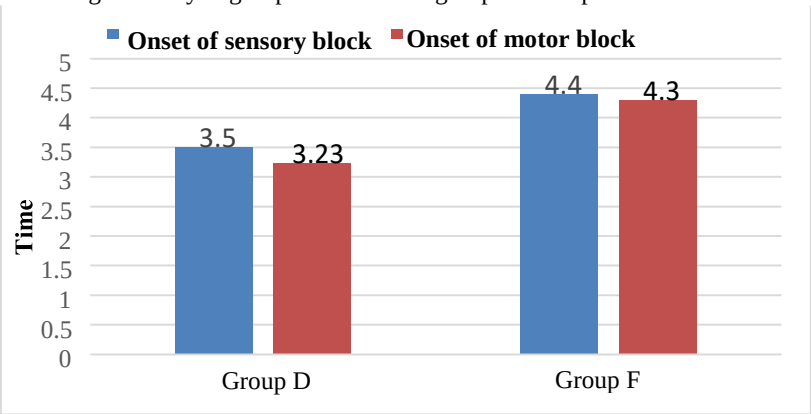

Figure 1- Time of onset of sensory block and motor block in both study groups

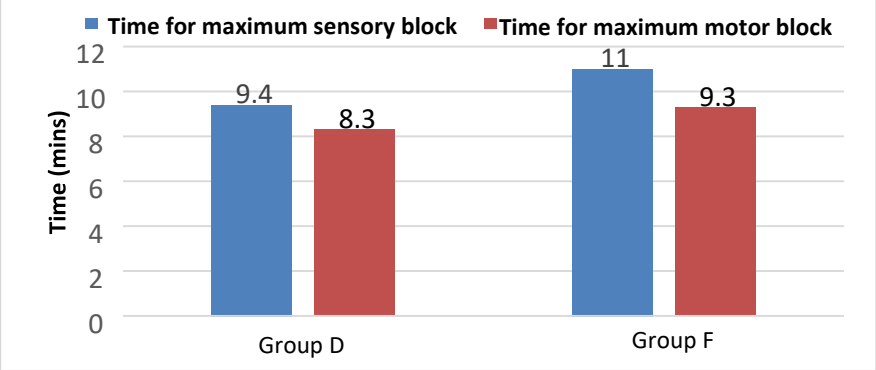

Figure 2- Time required for maximum sensory block and maximum motor block in both study groups

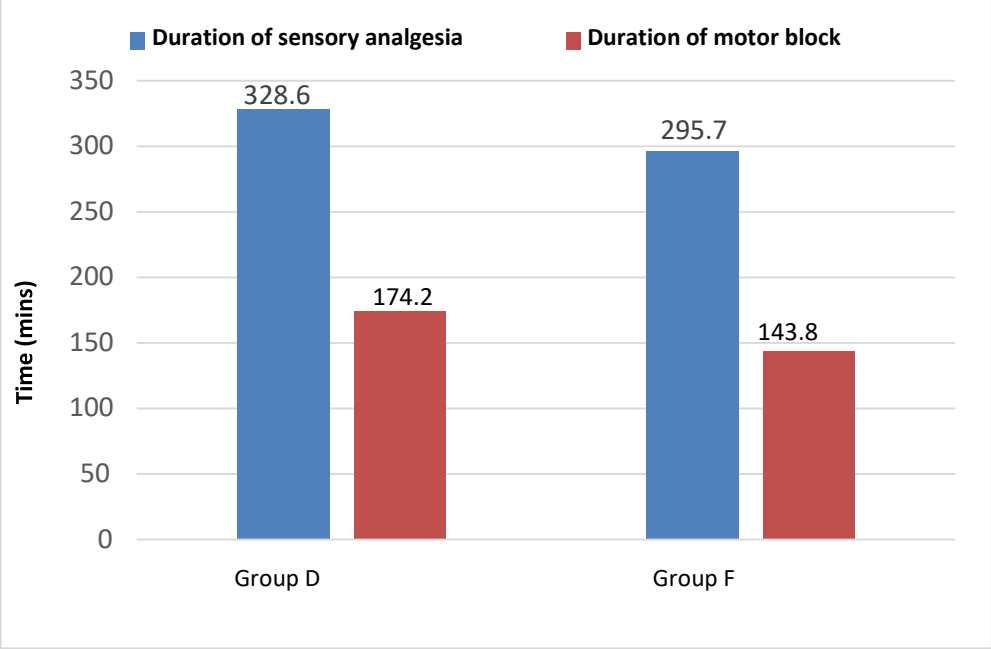

Figure 3- Duration of sensory analgesia and motor block in both study groups

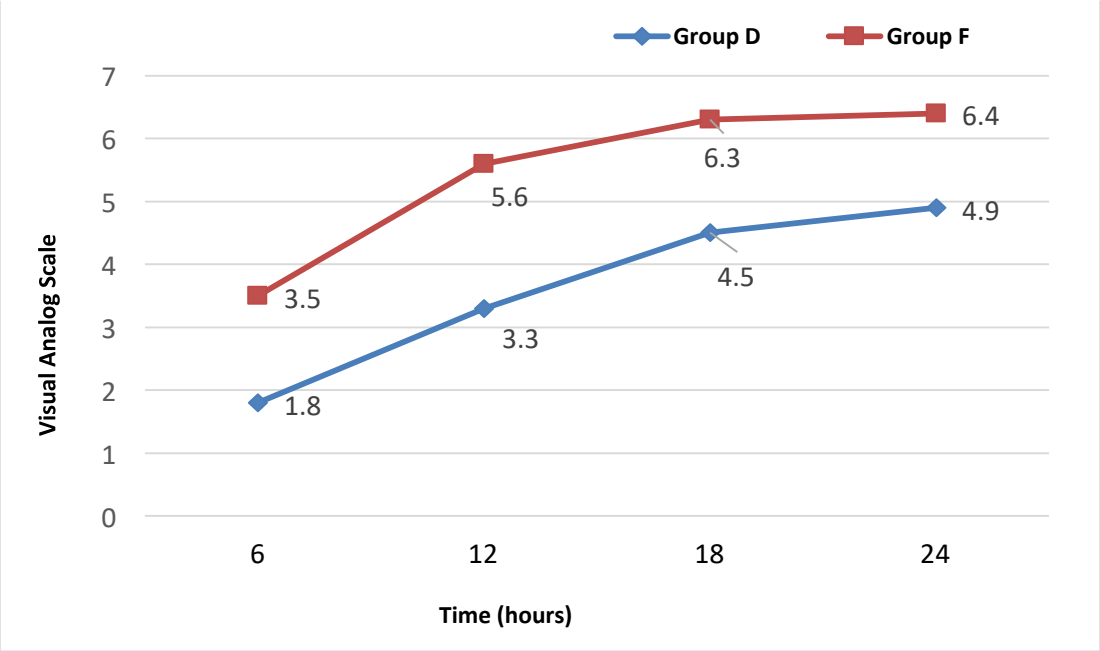

Figure 4- Comparison of post-operative pain using visual analogue score in two study groups

It was found that out of 50 patients 27 patients in group D requested for rescue analgesia only one time, 14 patients in group D and 2 patients in group F requested for 2nd analgesic dose, 5 patients in group D and 23 patients in group F requested for 3rd analgesic dose, 20 patients and 5 patients requested 4th and 5th dose of analgesic dose respectively. 4 patients in group D did not requested for any analgesic dose. From observation we found the mean analgesic dose in group D is 1.4 ± 0.78 and in group F is 3.6 ± 0.73. It has been observed that requirement of inj diclofenac sodium dose in first 24 hrs post operatively was significantly lower in group D as compared to group F ($p<0.005$).

In group D, nausea, vomiting and pruritus had not occurred in any patient (0%), bradycardia in 6 patients (12%), hypotension in 8 patients (16%) and 36 patient (72%) had not any side effect which is comparable to group F in which nausea vomiting and bradycardia was occurred in 1 patient each (2%), hypotension in 6 patient (12%), pruritus in 2 patients (4%) and 40 (80 %) patients had no side effects which was not statistically significant.

Discussion

Spinal anaesthesia has emerged as an important regional anaesthesia technique as it is simple to administer, effective, reliable, economic, and safe for lower abdominal surgeries. It possesses less risk of pulmonary aspiration with excellent muscle relaxation with additional benefits include reduction in metabolic response to surgery, reduction in blood loss, decreased incidence of thromboembolism, decreased pulmonary compromise particularly in patients with advanced pulmonary disease and ability to monitor patient's mental condition (alertness) during surgery [7].

Bupivacaine Hydrochloride is most used local anaesthetic in spinal anaesthesia. It is amide group of long-acting local anaesthetic acts by blocking voltage gated sodium channel on neuronal membrane there by interrupting initiation and propagation of impulse in axon and produce wide variety of sensory and motor blockade. It offers rapid onset of action, reliable surgical anaesthesia and good muscle relaxation. But these advantages are offset by relatively short duration of action and less post operative analgesic effect [2].

To improve the spinal anaesthetic efficacy, postoperative analgesia, to lower local anaesthetic dose requirements and to reduce dose-dependent side-effects, adjuvants from different pharmacological classes of drugs such as Opioids and α-2 agonists, Midazolam, Neostigmine, Ketamine, Magnesium sulfate are used. Fentanyl Citrate a lipophilic Mu- opioid receptor agonist, is used as an adjuvant, which prolongs the duration of spinal anaesthesia. Dexmedetomidine, a newer highly selective α–2 agonist drug having analgesic, sympatholytic, sedative, and hemodynamic stabilizing properties. When it is given intrathecally, can interrupt pain transmission by depressing pronociceptive transmitter from presynaptic C fibers and by hyperpolarizing postsyneptic dorsal horn neurons in spinal cord which significantly prolongs the duration of spinal anaesthesia, provide good postoperative analgesia

and it is found to have antinociceptive action for both somatic and visceral pain [8].

Demographic data was comparable in both the study group and supported by the studies conducted by Ahmed W et al [9], Rahimzadeh P at al. [10], Singh R Al,et al. [11], Taksande K L A et al [12] & Kuusniemi KS et al. [13]. The mean time for onset of sensory block in group D was (3.5 ± 0.88 mins) while in group F, it was (4.4 ± 1.2 mins). This difference was statistically significant(p=0.001). Ahmed W et al [9], also observed similar result in their study that sensory onset was significantly faster in group D than in groups F (P=0.000). Another study conducted by Taksande K L A et al (12) established that the mean onset of sensory block in group D was (6.70 ± 0.79 mins) while in group F. It was (8.03 ± 1.22 mins), and the difference was statistically significant.

In contrast to the present study, Al-Ghanem SM et al. [14] found no significant difference between the onset times of the different groups in their study when comparing Dexmedetomidine and Fentanyl as adjuvants to Bupivacaine in gynecological surgeries. The reason behind this contrasting result may be the isobaric Bupivacaine used in their study instead of hyperbaric Bupivacaine which was used in the present study. The mean time of onset of motor block in group D (3.23 ± 1.0mins) was significantly lower than in group F (4.3 ± 1.1 mins). A similar study conducted by Ahmed W et al [9] there was statistically significant difference between the three groups with conclusion of faster onset in group D compared with groups F which is again faster than control group B (P= 0.001). Fyneface-Ogan S et al [15] had found faster motor onset in the Dexmedetomidine group when compared with Fentanyl as adjuvants to intrathecal Bupivacaine on labor outcome. Al-Ghanem, et al. [14] observed in their study that time of onset of motor block was not different between Dexmedetomidine and Fentanyl group.

Duration of sensory block was significantly higher in group D (328.6± 66.5mins) as compared to group F (174.2 ± 21.9min) and duration of motor block in group D (295.7 ± 63.0mins) was significantly higher than in group F (143.8 ± 19.2mins). These results supported by the studies carried out by Al-Mustafa et al [16] and Al-Ghanem (14) et al., Mahendru et al. [17], Singh R et al. [11].

In present study, the mean sedation score was significantly higher in group D at 60 minutes (2.24 ± 0.47), 90minutes (2.38±0.53) and 120 minutes (2.18±0.38) intra-operatively as compared to patients in group F which was at 60 minutes (2.02 ± 0.14),90 minutes (2.04 ±0.19), 120minutes (2.0 ± 0). This observed difference was found to be statistically significant. Chattopadhyay I, et al [18] observed that no sedative effect of Dexmedetomidine during their study. In their study they observed sedation score <2 at every time which shows contrast with present study. Another study done by Sethi S et al [19], observed significantly higher mean sedation score in Group D at 25 min to 60 mins as compared with group M. Like present study this was statistically significant with p<0.001 but the score remains clinically acceptable range in both groups.

The mean analgesic dose in group D is 1.4 ±0.78 and in group F is 3.6 ± 0.73. It has been observed that requirement of inj.Diclofenac sodium dose in first 24 hrs. post operatively was significantly lower in group D as compared to group F (p<0.005). Like present study, Verma R et al [6] observed lower VAS score and less number of Diclofenac doses requirement in the first 24 hrs in the Dexmedetomidine group compared with the Fentanyl group. Similarly, Mahendru, et al [17] reported lower VAS values in the Dexmedetomidine group compared to Fentanyl group and Clonidine group in their study. Ahmed W et el [9] reported that the time to first analgesia request was significantly longer in group D in comparison with groups F (P = 0.013). Moreover, there was no need for rescue analgesia in 75% of patients in group D and in 50% of patients in group F. There was significantly reduced 24 h requirements of total analgesics (Pethidine and Diclofenac sodium) in group D compared with groups F.

The mean basal hemodynamic parameters were comparable in both the groups. After intrathecal injection, at 2 min, 4 min, 6 min and 8 min, 20 mins the heart rate decreased in both groups and it was significantly decreased in group D patients as compared to group F although after 30 mins, the heart rate remained stable and comparable in both the study groups. There was no statistically significant difference in two groups with respect to heart rate and these results were supported by the study conducted by, Eid HE et al [20] and Debabrata, et al [21]. Mean SBP was decreased after intrathecal injection in both groups during 2 mins to 90 mins which was significant in group D compared with group F. However, fall in mean SBP was not statistically significant at 20 mins and 40 mins in group D as compared to group F. Both groups showed fall in DBP initially from 2 mins to 40 mins. with no statistically significant. Both groups showed fall in MAP initially from 2 mins to 40 mins. with no statistical significance. In agreement with the present study, Al Ghanen, et al [14] demonstrated significant decrease in HR and MAP on comparing the addition of 5 mcg Dexmedetomidine with intrathecal Bupivacaine with 25 mcg fentanyl in gynecological procedure. Like present study, Malawat A et al [7] in their study showed that hemodynamic parameter was found to be well maintained without any significant difference in Dexmedetomidine group and Fentanyl group when used with adjuvant with Bupivacaine in lower limb surgeries for spinal anaesthesia. The hemodynamic parameters, as evident from different studies including this study, remained

stable throughout the study period which confirms the established effects of α-2 agonist on hemodynamics.

Ahmed W et al [9] reported side effects such as nausea, vomiting, shivering, pruritus, respiratory depression, and sedation after addition of Dexmedetomidine and Fentanyl to spinal anaesthesia but found to be not significant as similar with present study. In contrast to present study, Singh R et el [11] reported relatively higher proportion of patients in Dexmedetomidine (5mcg) group showed bradycardia (17.5%) as compared to Fentanyl (25mcg) supplemented group (5%).

Conclusion

From this study, we observed that patients who were administered Dexmedetomidine as an adjuvant to intrathecal Bupivacaine showed early onset of sensory and motor block as well as prolonged duration of sensory analgesia and motor block compared to those who had been administered Fentanyl with Bupivacaine. Better sedation, good quality of postoperative analgesia with less consumption of post operative analgesics and better hemodynamic stability without any severe side effect also observed with Dexmedetomidine compared to Fentanyl. Hence, we concluded that Dexmedetomidine is a better adjuvant than Fentanyl as far as rapid onset and prolonged sensory and motor block, patient comfort, stable hemodynamic parameters, quality of intra operative and post-operative analgesia is concerned.

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