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Original Research Article

A Comparative Evaluation of Dexmedetomidine and Fentanyl as Adjuncts to Bupivacaine in Intrathecal Anaesthesia

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Abstract:

Introduction: To enhance spinal anaesthetic efficacy, adjuvants from different pharmacological classes of drugs are used to augment and prolong analgesia. Dexmedetomidine, a α_2-adrenoceptor agonist acts by binding to presynaptic C-fibers and postsynaptic dorsal horn neurons. Fentanyl is a lipophilic μ-receptor-agonist opioid it exerts its effect by combining with opioid receptors in the dorsal horn of the spinal cord and may have a supraspinal spread and action.

Aim: A Comparative Evaluation of Dexmedetomidine and Fentanyl as Adjuncts to Bupivacaine in Intrathecal Anaesthesia.

Methodology: A prospective, comparative randomized, double-blinded study was performed on 60 patients. These 60 patients were divided into 2 groups Group dexmedetomidine (n = 30) and Group fentanyl (n = 30) and were compared for onset of analgesia, motor blockade, total duration of anaesthesia, sedation score, hemodynamic variables and postoperative side effects.

Result: The mean time of onset of sensory block in group D was 3.9±0.70 min, and in group F it was 5.1±0.79 min. The difference was statistically significant. The mean time of onset of motor block in group D was 4.8±0.83 min, and in group F it was 5.75±0.69 min. The difference was statistically insignificant. The duration of analgesia in group D was 486.6±23.13 min and 296.33±25.16 min in group F. The difference was statistically significant. The duration of motor block in group D was 419.7±10.24 min and 160.36±6.37 min in group F. The difference was statistically significant.

Conclusion: Dexmedetomidine is a better adjuvant than fentanyl in spinal anaesthesia as far as patient comfort, stable cardio-respiratory parameters, and intra-operative and post-operative analgesia are concerned.

Keywords: Dexmedetomidine, Fentanyl, Adjuncts, Bupivacaine, Intrathecal Anaesthesia.

Introduction

The amelioration of agonizing pain has been the substantial goal of anaesthesia. With the enlightenment of anatomy, physiology, pharmacology, and technical skills, the anaesthesiologists are the premier physicians to cure pain. Spinal anaesthesia has been endorsed as one of the regional anaesthesia techniques as it is easy to administer, produces rapid onset of anaesthesia and complete muscle relaxation, has superior blockade, has lower failure rates, and is also economical.

To enhance spinal anaesthetic efficacy, adjuvants from different pharmacological classes of drugs are used to augment and prolong analgesia, to lower dose requirements, and to reduce dose-dependent side effects of local anaesthetics. Postoperative analgesia has always been a domain of concern for surgeons as well as anaesthesiologist. The postoperative period plays an imperative role in surgical outcomes and patient welfare. Hyperbaric bupivacaine is the most widely used long-acting regional anaesthetic agent, but the limitation of its use alone is that it has a limited postoperative analgesia duration. Hence, various adjuvants have been amalgamated with local anaesthetic agents to increase the duration of analgesia. To sustain the advantage of low-dose bupivacaine while improving the intraoperative quality of anaesthesia, different agents such as epinephrine, phenylephrine, ketamine, benzodiazepines, neostigmine, opioids, and magnesium sulfate have been used as adjuvants for prolonging the duration of spinal anaesthesia.

In the present study, an attempt was made to compare the analgesic effects, duration of anaesthesia, and side-effects of dexmedetomidine and fentanyl when used as adjuvants with bupivacaine in patients undergoing lower abdominal surgeries.

Dexmedetomidine, a α_2-adrenoceptor agonist, has been approved by the Food and Drug Administration (FDA) as a short-term sedative for mechanically ventilated intensive care unit (ICU) patients. It acts by binding to presynaptic C-fibers and postsynaptic dorsal horn neurons.

Fentanyl is a lipophilic μ-receptor-agonist opioid. Intrathecally, fentanyl exerts its effect by combining with opioid receptors in the dorsal horn of the spinal cord and may have a supraspinal spread and action.

Materials and Methods

After obtaining institutional ethical committee approval, this prospective randomized double-blinded study was carried out in the Department of Anaesthesiology, Government Medical College Kota, from January 2018 to April 2019 on 60 patients of both sexes.

Inclusion criteria: Patients with ASA I or II and an age group of between 20 and 60 years who are undergoing elective lower abdominal and lower limb surgeries.

Exclusion criteria: Patients refusal for spinal anaesthesia**,** local infection at the injection site**,** neurogenic pain**,** neurological deficit**,** coagulopathy**,** patients known to be sensitive to or allergic to dexmedetomidine, fentanyl, or Bupivacaine, Patients with a history of cardiac or respiratory diseases; patients on beta-adrenergic blockers, calcium channel blockers, and ACE inhibitor treatment; and psychiatric patients.

Sample size calculation with justification: Based on a minimum mean difference of 25% in parameters with α =0.01 and β = 0.20, the sample size for each group was estimated to be 28. Rounding up this figure, we included 30 patients in each group. The sample size has been calculated using MedCalc Software version 11.5.0.0.

The patients were randomly allocated into two groups by using 'computer-generated random numbers'. Cases were selected on the basis of a simple random sampling method and were randomly allocated into two groups of 30 patients each, as follows:

Group Dexmedetomidine (n=30): patients received a combination of 5 μg of Dexmedetomidine in 0.5 ml of normal saline and 2.5 mL of 0.5% Bupivacaine intrathecally.

Group Fentanyl (n=30): patients received a combination of Fentanyl 25 μg in 0.5 ml and 2.5 ml of 0.5% Bupivacaine intrathecally.

Routine and required special investigations were carried out. A preoperatively detailed history and clinical examination were done, and written informed consent was obtained. The entire anaesthetic procedure, including the drugs used, was explained to the patient. On the day of surgery, confirmation of NPO status according to ASA guidelines, investigations, and standard anaesthetic trolleys, including emergency drugs and airways, were checked. Base-line vitals were recorded. The intravenous line was secured, and patients were given 15 mL/kg ringer lactate as preloading. Monitors were attached according to ASA guidelines.

The patient was positioned in the sitting position, and after adequate aseptic precautions, a lumbar puncture was performed at L3/L4 or L2/L3 intervertebral space using a midline approach with a 25-gauge Quincke spinal needle. After ensuring a free flow of CSF, the drug was injected. According to the administered concentration of the drug, patients were grouped into Group D and Group F.

We assessed the onset and duration of analgesia, the onset and duration of motor blockade, the total duration of spinal anaesthesia, sedation score, hemodynamic variation in the intra- and postoperative period, analgesic requirements, and postoperative complications such as nausea, vomiting, hypotension, bradycardia, and depression of ventilation. All patients were observed in the postoperative period. The intensity of pain was measured using a 10-cm visual analogue scale (VAS) at a half-hourly interval. The pain-free postoperative interval was observed and recorded. Rescue analgesia was provided by an intravenous infusion of 50–100 mg of tramadol when the VAS score was 4 or higher. All patients were observed for 24 hours postoperatively for any complaints of pruritus, nausea, vomiting, hypotension, bradycardia, respiratory depression, and post-spinal shivering. Intraoperative and postoperative complications were noted and managed accordingly.

The results were statistically analysed using SPSS (Statistical Package for Social Science) software version 15.0. A chi-square test was used for qualitative data (age, sex, ASA grade, VAS score). Quantitative data among the two groups were compared using an unpaired student t-test. Heart rate and mean arterial pressure were compared within the group against baseline values using a student (paired) t-test. A $P < 0.05$ was considered as significant.

Results: There was no significant difference in demographic data, which included patient age, sex, weight, and ASA grading, among both groups.

Table 1:

	Group D	Group F	P-value
Age (years)	41.4±12.1	40.4±11.5	0.807
Sex (M:F)	12:18	19:11	
Weight (Kg)	61.3±4.76	61.13±4.67	0.9
ASA GRADE	18:12	20:10	

The mean time of onset of sensory block in group D was 3.9±0.70 min, and in group F it was 5.1±0.79 min. The difference was statistically significant. The mean time of onset of motor block in group D was 4.8±0.83 min, and in group F it was 5.75±0.69 min. The difference was statistically insignificant.

Table 2:

Onset time	Group D	Group F	P-value
Sensory	3.9±0.70	5.1±0.79	0.021
Motor	4.8±0.83	5.75±0.69	0.091

The mean time to reach the highest sensory level in group D was 8.2±0.88 minutes and in group F was 11.9±0.7 minutes, with a p value of 0.011, which is statistically significant.

The mean time taken for two-segment regression in group D was 139±2.75 minutes and in group F was 88.5±4.1 minutes, with a p value of 0.001, which is statistically significant.

The mean time taken for regression to the S2 segment in group D was 476±10.53 minutes, and in group F it was 187±6.31 minutes, with a p value of 0.001, which is statistically significant.

Table 3:

Times in minutes	Group D	Group F	P-value
Time to reach highest sensory level	8.2±0.88	11.9±0.7	0.011
Time to 2 segment regression	139±2.75	88.5±4.1	0.001
Time to sensory regression to s2 segment	476±10.53	187±6.31	0.001

The duration of analgesia in group D was 486.6±23.13 min and 296.33±25.16 min in group F. The difference was statistically significant. The duration of motor block in group D was 419.7±10.24 min and 160.36±6.37 min in group F. The difference was statistically significant.

Table 4:

Times in minutes	Group D	Group F	P-value
Duration of analgesia	486.6±23.13	296.33±25.16	0.001
Duration of motor block	419.7±10.24	160.36±6.37	0.001

The distribution of patients according to their highest sensory level was comparable in both groups.

Table 5:

Highest sensory level	Group D		Group F	
	n	%	n	%
T4	3	10	1	3.3
T5	8	26.7	7	23.3
T6	12	40	17	56.7
T7	4	13.3	3	10
T8	3	10	2	6.7
Total	30	100	30	100

Changes in heart rate (beats per minute): On intergroup comparison, the heart rate was significantly lower in group D after 10 minutes and remained low up to 1 hour in group D as compared to group F. After that, there was no significant difference in the mean heart rate between the two groups.

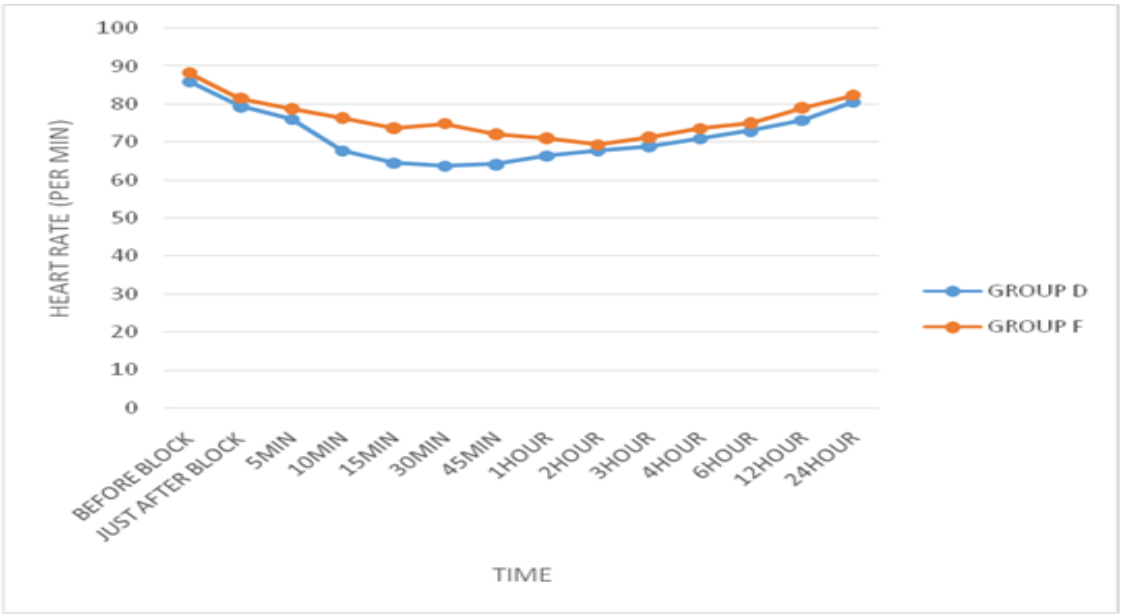

Figure 1:

Changes in mean arterial blood pressure (MAP) in mmHg: On intergroup comparison, the mean arterial blood pressure was significantly lower in group D after 15 minutes and remained low up to 1 hour in group D as compared to group F. After that, there was no significant difference in mean arterial blood pressure between the two groups.

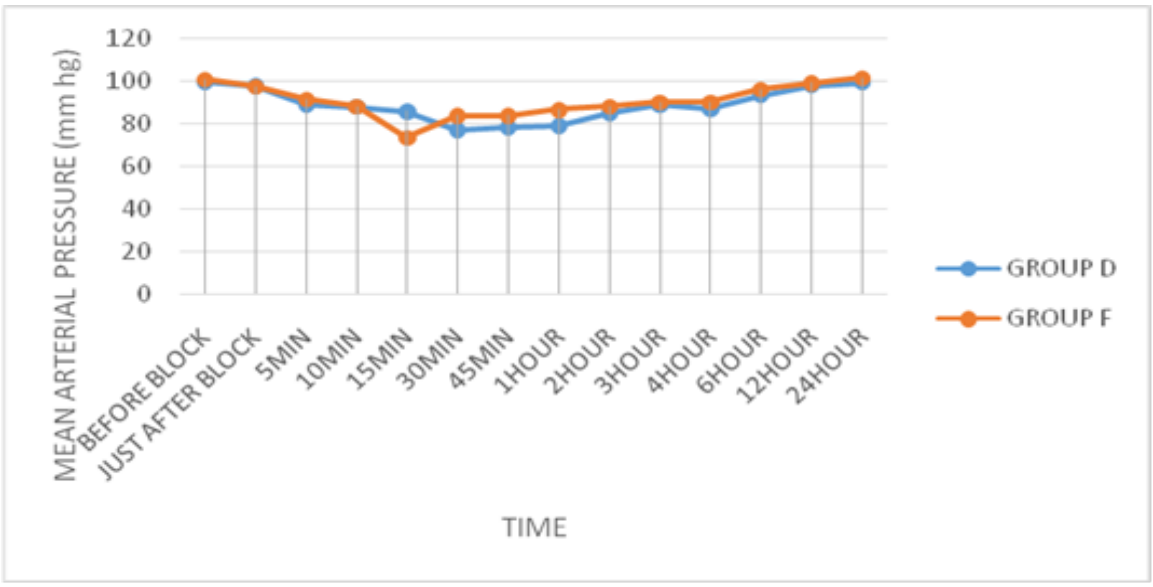

Figure 2:

Oxygen Saturation (SPO2) % : The mean of SPO_2 was comparable among both groups.

Respiratory rate: The respiratory rate was comparable in groups D and F.

Changes in VAS score: The VAS score in group D was lower as compared to group F at all-time intervals.

The VAS score is highly significant at 4 and 6 hours after the spinal block. The VAS score is comparable across time intervals.

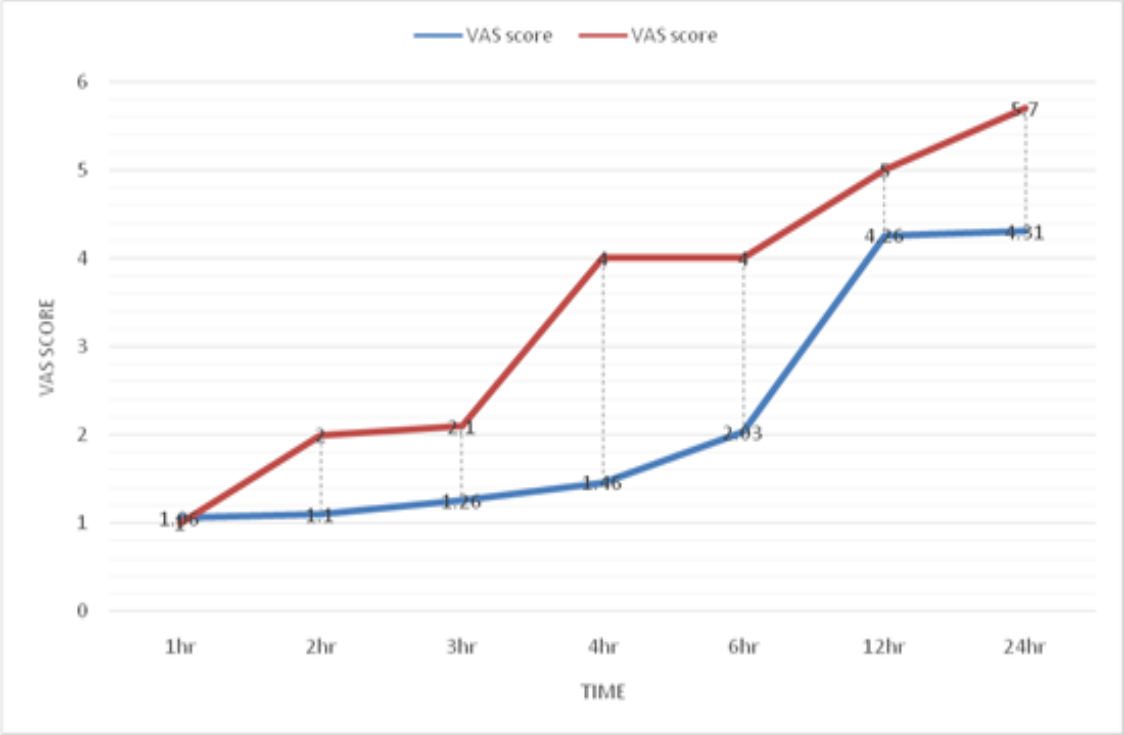

Figure 3:

Changes in sedation score: Changes in sedation score in groups D and F from baseline until the end of the procedure were monitored every 15 minutes until 1 hour, then hourly. The session score was statistically significant at the 1st and 2nd hours among both groups. Sedation scores were comparable in the rest of the time intervals.

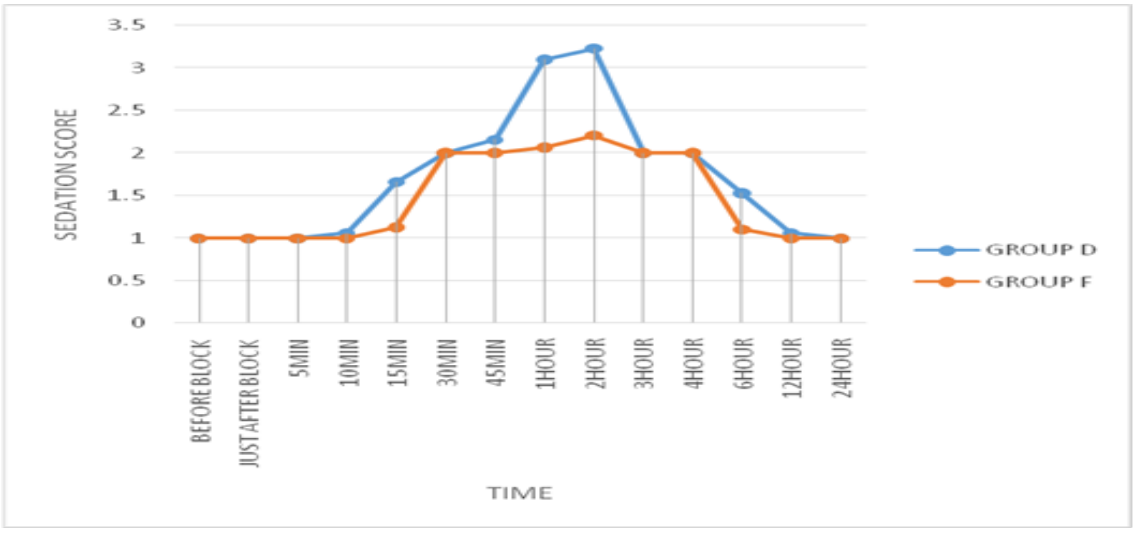

Figure 4:

Side effects- The incidence of side effects was comparable (p >0.05).

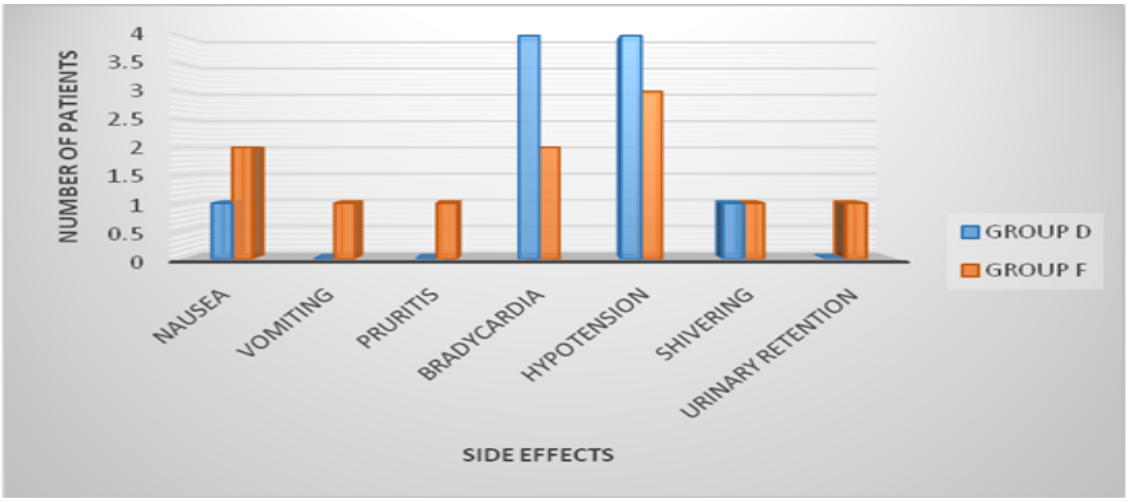

Figure 5:

Discussion

Sensory Block Characteristics

Onset of analgesia: Our study showed the duration of analgesia was 3.9±0.70 min in group D and 5.1±0.79 min in group F. The onset of sensory loss was faster in group D than in group F. The difference was statistically significant (P = 0.021). Senthilet al [1], also observed a significantly faster onset of sensory loss in group D patients as compared to group F patients.

Time to reach the highest sensory level: The mean time to reach the highest sensory level in group D was 8.2±0.88 min, and in group F it was 11.9±0.7 min, with a p value of 0.011, which was statistically significant. In accordance with our result, Senthilet al [1] and El Attar et al [2] also observed a significantly shorter time to reach the highest sensory level in patients who had dexmedetomidine in comparison to the fentanyl group.

Highest sensory level: In the present study, the highest mean sensory block was achieved up to the T6 spinal segment, with a range of T4 to T8 spinal segments in both groups.

Similarly, Ghanemet al [3] also noted the mean highest sensory block level up to the T6 spinal segment. However, Gupta R et al [4] obtained the mean highest sensory level up to T5 (T4-T8) and T6 (T4-T7) spinal segments in the dexmedetomidine and fentanyl groups, respectively.

Time of two segment regression: In our study, we observed that the mean time taken for two-segment regression in group D was 139 ± 2.75 min, and in group F, it was 88.50 ± 4.1 min, with a p value of <0.001, which is statistically significant. Our study was also comparable with the study conducted by Khan Aamir Laique et al [5], in which two-segment regression in group D was 129.50 ± 9.04 min and in group F was 77.50 ± 7.42 min with p <0.001.

Time to sensory regression to S2 spinal segment: It was observed in our study that the mean time taken for regression to the S2 spinal segment in group D was 476 ± 10.53 min and in group F was 187 ± 6.31 min, with a p value of <0.001, which is statistically significant. Al-Mustafa et al [6], noted a regression time to S2 of 165.5±32.9 min with plain bupivacaine and 277.1±23.2 min with 5µg and 338.9±44.8 minutes with 10µg dexmedetomidine with bupivacaine, respectively, with a p value of <0.001. Similar results were also observed in the studies of Wafiyaet al [7] and Ogan et al [8].

Duration of analgesia: In our study, we found a highly significant difference regarding the duration of analgesia, with the dexmedetomidine group having 486.6±23.13 min of duration of analgesia compared to the fentanyl group having 296.33±25.16 min. Our results also coincide with the results of Tarbeehet al [9], where the fentanyl group had duration of analgesia of 280 ± 62 min in comparison to 450 ± 75 min in the dexmedetomidine group. Similarly, our study is also comparable to the study conducted by Chandak A et al [10]. In their study, the duration of analgesia in the dexmedetomidine group was 321±24 min and in the fentanyl group was 288.75±14.67 min.

Motor Block Characteristic

Onset of the motor block: In our study, the mean time taken for the onset of motor block in group D was 4.8±0.83 min, and in group F it was 5.75±0.69 min, with a p value of 0.091, which was insignificant. The onset time of motor block in a study conducted by Gupta R et al [4], was 11.6±1.8 min and 11.2±1.3 min for the dexmedetomidine and fentanyl groups, respectively, with a p value of 0.14 (not significant). Ghanem et al [3], noted a motor block onset time of 14.4±6.7 minutes and 14.3±5.7 minutes for the dexmedetomidine and fentanyl groups, respectively, with a p value of 0.932 (not significant). Our results are also in accordance with

Fernandez et al [11], Mahdy et al [7] and Chandak AA et al [10].

Duration of the motor block: In our study, the duration of motor block in group D was 419.7±10.24 min and 160.36±6.37 min in group F, with a p value of 0.001, which was significant. Our results are comparable with the study conducted by Gupta R et al [4], where the dexmedetomidine group had duration of motor block of 421±21 min as compared to 149.3±18.2 min in the fentanyl group. Al-Ghanemet al [3] also found a significantly longer duration of motor block in the dexmedetomidine group (240±64) min as compared to the fentanyl group (155±46 min). However, the duration of motor block in their study was less as compared to our study, as isobaric bupivacaine 10 mg was used in their study compared to 12.5 mg of hyperbaric bupivacaine used in our study. Similar results were also noted in the studies of Wafiyaet al [7].

Cardio-Respiratory Parameters

Mean heart rate: Regarding heart rate, the fall in mean heart rate as compared to basal heart rate was greater in group D in comparison with group F during the intra-operative period up to 60 minutes, and it was statistically significant ($p < 0.05$). In a study conducted by Mohammed et al [12], they observed that the mean intraoperative heart rate reduced significantly in the dexmedetomidine group with a p value of <0.05 compared with the fentanyl and plain bupivacaine groups.

After 1 hour, there was no significant difference in mean heart rate between the two groups.

The difference in mean heart rate was statistically significant from the baseline value (p value < 0.05) at all the time intervals in both groups.

Although a significant fall in heart rate was observed in both groups, this fall was within acceptable limits. Only 4 patients in group D and 2 patients in group F out of 30 patients in each group received atropine due to a decrease in heart rate of <50 bpm. These results suggest the established effects of dexmedetomidine and fentanyl in providing hemodynamically stable perioperative and postoperative periods.

Mean arterial blood pressure: our study results have shown that a significant fall in mean arterial blood pressure occurred in patients receiving dexmedetomidine and fentanyl as adjuvants in the intra-operative period and post-operative period up to 45–60 minutes. The mean arterial blood pressure was significantly lower in group D after 15 minutes and remained low up to 1 hour in group D as compared to group F (p value < 0.05). After that, there was no significant difference in mean arterial blood pressure between the two groups. The difference in mean arterial blood pressure was statistically significant from the baseline value (p value < 0.05) from a 5 min- to 6-hour time interval in group D. The difference in mean arterial blood pressure was statistically significant from the baseline value (p value 0.05) from a 5 min to 4-hour time interval in group F.

In spite of the fall in MAP, only 4 patients out of 30 in group D and 3 patients out of 30 in group F received vasopressors due to a fall in MAP >20% of the baseline value. That suggests that although both dexmedetomidine and fentanyl cause a fall in MAP and set the MAP at a lower normal limit that does not make the patient hemodynamically unstable.

The results of our study correlate with those of Gupta R et al [4], Chandak A et al [10], who found that both additives cause a fall in blood pressure and a fall in heart rate, and this fall was greater in the dexmedetomidine group as compared to the fentanyl group, but that does not make patients hemodynamically unstable.

Mean oxygen saturation: In both groups, changes in mean oxygen saturation during the intraoperative and postoperative periods remained statistically insignificant ($p > 0.05$), suggesting no hypoxic episode in any of the patients included in the study during the whole course of the study period.

Changes in respiratory rate (bpm): In both groups, changes in respiratory rate (bpm) during the intraoperative and postoperative periods remained statistically insignificant ($p > 0.05$), suggesting no respiratory depression episode in any of the patients included in the study during the whole course of the study period.

Similar to our study, Ghanem et al [3], Mustafa et al [6] and Biswas et al [13], Wafiyaet al [7], Tarbeeh et al [9] and Ogan et al [8], did not find any significant difference in oxygen saturation or respiratory rate compared to baseline in both the dexmedetomidine and fentanyl groups.

Changes in VAS Score:

In our study, VAS scores during the postoperative 24-hour period were significantly lower in group D as compared to group F.

Similar results were observed by Tarbeehet al [9] who also recorded a significantly lower VAS score in patients who received dexmedetomidine compared to patients who had intrathecal fentanyl.

Intra-Operative Sedation Score: In our study, all the patients in both groups had a mean sedation score of 2 or 3. The changes in sedation scores in both groups were statistically significant at the 1st and 2nd hours after spinal block among both groups, with a p value of <0.05. The mean sedation score in group D at 1 hour was 3.1 ± 0.30 and in group F was 2.06 ± 0.25.

Wafiyaet al [7] noted a mean sedation scale of 3.2±0.50 in the dexmedetomidine group, 2.2±0.23 in the fentanyl group, and 1.0±0.3 in the control group, which was also statistically significant. In our study, Group D, compared to Group F, caused a significant fall in the sedation scores at the 1st and 2nd hours after spinal block. Sedation scores were comparable in the rest of the time intervals.

Side effects: In our study, we observed side effects like nausea, vomiting, hypotension, bradycardia, a decrease in saturation, pruritis, and other side effects like shivering during the intraoperative and postoperative periods, which required intervention.

However, the incidence of side effects was comparable ($p > 0.05$). Similar observations were noted in the studies of Gupta R et al [4], Ghanem et al [3], Mustafa et al [6], Biswas et al [13], Mohammed et al [12], Tarbeeh et al [9], Ogan et al [8] and Wafiya et al [7].

In our study comparing intrathecal dexmedetomidine and intrathecal fentanyl with bupivacaine, the results indicate that dexmedetomidine provides better sensory and motor blockade when compared to fentanyl. The hemodynamic stability and side effects were similar in both groups.

Conclusion

Alpha-2 adrenergic agonist dexmedetomidine intrathecally with hyperbaric bupivacaine significantly prolongs the duration of sensory and motor blockade and the duration of analgesia. Dexmedetomidine is a better adjuvant than fentanyl in spinal anaesthesia as far as patient comfort, stable cardio-respiratory parameters, and intra-operative and post-operative analgesia are concerned. Overall, the experience with dexmedetomidine was quite satisfactory as compared to fentanyl because of its superior sedative and anxiolytic properties during the surgical procedure under regional anaesthesia. Use of dexmedetomidine as an adjuvant is an alternative to achieve an anaesthetics quality that keeps the patient in a state of active sedation, which reduces the likelihood of respiratory depression, which can arise when adjuvant drugs are administered intravenously.

Bibliography

1. Senthil, Chitraleka. S. Comparison of dexmedetomidine and fentanyl as intrathecal adjuvants to hyperbaric bupivacaine for total abdominal hysterectomy under subarachnoid block. Ind J of Applied Research. (2019)9,9
2. El- Attar Ahmed, Aleem M A, Beltagy R, et al. A comparative study of intrathecal dexmeditomidine and fentanyl as additives to bupivacaine. Research and Opinion in Anesthesia and Intensive Care.2015;2:43-49.
3. Al Ghanem SM, Massad IM, Al-Mustafa MM, et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedures: A double blind controlled study. Am J Appl Sci 2009; 6:882-7.
4. Gupta R, Verma R, Bogra J, et al. A comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesthesiol Clin Pharmacol 2011; 27:339-43.
5. AamirLaique Khan, Raj Bahadur Singh, et al. comparative study between intrathecal dexmedetomidine and fentanyl as adjuvantto intrathecal bupivacaine in lower abdominal surgeries. Anesth Essays Res. 2015 May-Aug; 9(2): 139–148.
6. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J 2009; 30:365-70.
7. Mahdy W R, Abdullah S I. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics and neonatal outcome in uncomplicated caesarean delivery. MMJ Jan 2011; 24 (1); 221–32.
8. Ogan S F, Job O G, Enyindah C E. Comparative Effects of Single Shot Intrathecal Bupivacaine with Dexmedetomidine and Bupivacaine with Fentanyl on Labor Outcome. ISRN Anesthesiology. 2012:1-6, Article ID 816984.
9. Tarbeeh G A, Mohamed A A. Effects of intrathecal bupivacaine-fentanyl versus bupivacaine-dexmedetomidine in diabetic surgical patients. Egyptian Journal of Anaesthesia (2013) 29, 13-18.
10. Chandak A, Thaker J A, Kapdi M S. A Comparative Study of Bupivacaine, Bupivacaine with Dexmedetomidine and Bupivacaine with Fentanyl in Spinal Anaesthesia for Lower Abdominal Surgery. International J Scientific Res 2013; 2(6): ISSN No 2277 – 8179: 422-24.
11. Fernandez-Galinski D, Rué M, Moral V, Castells C, Puig MM et al. Spinal anaesthesia with bupivacaine and fentanyl in geriatric patients. AnesthAnalg 1996; 83: 537-41.
12. Mohamed AA, Fares KM, Mohamed SA et al. Efficacy of intrathecally administered dexmedetomidine versus dexmedetomidine with fentanyl in patients undergoing major abdominal cancer surgery. Pain Physician 2012; 15: 339-48.
13. Biswaas BN, Rudra A, Bose BK, Nath S, et al. Intrathecal Fentanyl with Hyperbaric Bupivacaine Improves Analgesia During Caesarean Delivery And In Early Post-Operative Period. Indian J Anaesth 2002; 46(6): 469-472.