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EFFECT OF ADDING DEXMEDETOMIDINE VERSUS FENTANYL TO INTRATHECAL HYPERBARIC BUPIVACAINE ON SPINAL BLOCK FOR INFRAUMBILICAL ELECTIVE SURGERIES

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Abstract

Background: This study was conducted to compare the two adjuvant agents, dexmedetomidine (5µg) and fentanyl (25µg) added to 15mg of 0.5% hyperbaric bupivacaine introduced intrathecally for infraumbilical surgeries.

Methods: This was a hospital-based prospective, randomized clinical study conducted among 90 adult patients belonging to ASA Grades I and II of either sex undergoing elective infra-umbilical surgeries. The study was carried out in a tertiary care centre in the Department of Anaesthesiology of the Medical College and Hospital, from November 2011 to June 2013 after obtaining clearance from the institutional ethics committee and written informed consent from the study participants.

Results: The mean time to achieve sensory regression to the T12 level in group C was shorter as compared to groups F and D and these differences were found to be highly significant statistically. The difference in the results between group D and group F was statistically significant, with group D having a longer duration of sensory block. The differences in mean duration of complete motor block, complete analgesia, and mean time of rescue analgesia between the three groups were found to be statistically highly significant. Thus, dexmedetomidine (group D) has a longer duration than bupivacaine (group C) and fentanyl (group F).

Conclusion: Dexmedetomidine as an adjuvant significantly prolongs the duration of complete analgesia and the time of rescue analgesia as compared to fentanyl and bupivacaine. The

postoperative analgesic requirement was less for dexmedetomidine as compared to fentanyl and bupivacaine, leading to improved quality of analgesia.

Keywords: Dexmedetomidine, Fentanyl, Intrathecal Hyperbaric Bupivacaine, Spinal Block, Infraumbilical Elective Surgeries

INTRODUCTION

In order to maximise the duration of anaesthesia and postoperative analgesia, a number of adjuvants were added to local anaesthetics, such as opioids (morphine, fentanyl), vasoconstrictors (adrenaline), ketamine, midazolam, clonidine, etc., to name a few. It has been shown that there is a favourable outcome regarding the speed of onset, improved quality of anaesthesia, and duration of post-operative analgesia with the addition of these adjuvants. Sedation, stable hemodynamics, and the ability to provide smooth and prolonged postoperative analgesia are the main desirable qualities of an adjuvant in neuraxial anesthesia.[1]

Aims and Objectives

1. To study the effect of adding dexmedetomidine versus fentanyl to intrathecal hyperbaric bupivacaine on spinal block for infraumbilical elective surgeries with regard to onset of sensory block, onset of motor block, time to achieve maximum sensory block, time to achieve maximum motor block, maximum dermatomal level achieved, time of two-segment regression, time of regression to T12 and total duration of motor block.
2. To study and compare the hemodynamic changes between the three groups.
3. To study the incidence of side effects between the three groups.
4. To study and compare the duration of analgesia and post-operative analgesia required between the three groups.

MATERIALS & METHODS

This was a hospital-based prospective, randomized clinical study conducted among 90 adult patients belonging to ASA Grades I and II of either sex undergoing elective infra-umbilical surgeries. The study was carried out in a tertiary care centre in the Department of Anaesthesiology of the Medical College and Hospital, from November 2011 to June 2013 after obtaining clearance from the institutional ethics committee and written informed consent from the study participants.

Inclusion Criteria

- ASA grade I or II of either sex.
- Age between 18 and 60 years.
- Height between 150 and 170 cm.
- Patient undergoing elective infra-umbilical surgeries.
- Patient willing to undergo surgery under regional anaesthesia

Exclusion Criteria

- ASA grade III or IV
- Patients not willing for the procedure.
- Contraindications to spinal or epidural anaesthesia, e.g., bleeding diathesis, local infection and patients on anticoagulants.
- Height: <150 cm.
- Patient with spinal deformities.
- History of hypersensitivity to any opioid or local anaesthetic agent.
- History of neurological diseases and deformities.
- Patient on α2 antagonist therapy.
- History of cardiovascular diseases like hypertension, arrhythmias, and ischemic heart disease.

- Liver, respiratory, kidney, and endocrine diseases.
- Pregnant patients.

Statistical Methods

Parametric and non-parametric data were collected and entered in a master chart in a 2007 Microsoft Excel worksheet. All continuous variables (demographic and hemodynamic parameters) were presented as the mean ± SD.

RESULTS

Time (min)	**Group C**	**Group D**	**Group F**
90-120	4 (13.3%)	0 (0%)	0 (0%)
121-150	24 (80%)	0 (0%)	6 (20%)
151-180	2 (6.7%)	3 (10%)	19 (63.3%)
181-210	0 (0%)	17 (56.7%)	5 (16.7%)
211-240	0 (0%)	10 (33.3%)	0 (0%)
TOTAL	30 (100%)	30 (100%)	30 (100%)
MEAN ± SD	139.5 ± 13.60 min	208.116 ± 16.21 min	169.66 ± 13.76 min
One-Way ANOVA	**F= 167.23 , P<0.001, HS**		
Multiple Comparison	Group C vs. Group D	Group C vs. Group F	Group D vs. Group F
p-value	<0.001, HS	<0.001, HS	<0.001, HS
Comparison of Time of Regression to T12			
P-value is significant if < 0.05 and highly significant if < 0.001			
Time (min)	**Group C**	**Group D**	**Group F**
150-180	18 (60%)	0 (0%)	2 (6.7%)
181-210	12 (40%)	0 (0%)	16 (53.3%)
211-240	0 (0%)	6 (20%)	12 (40%)
241-270	0 (0%)	15 (50%)	0 (0%)
271-300	0 (0%)	9 (30%)	0 (0%)
TOTAL	30 (100%)	30 (100%)	30 (100%)
MEAN ± SD	179.16 ± 14.62 min	265.66 ± 19.24 min	209.66 ± 14.73 min
One-Way ANOVA	**F= 216.18 , P<0.001, HS**		
Multiple Comparison	Group C vs. Group D	Group C vs. Group F	Group D vs. Group F
p-value	<0.001, HS	<0.001, HS	<0.001, HS
Comparison of Total Duration of Complete Motor Blockade			
P-value is significant if < 0.05 and highly significant if < 0.001.			
Table 1			

It was defined as the time taken for the sensory level to regress from the highest levels to dermatome level T12. In 30 (100%) patients in group C, 3 (10%) patients in group D and 25 (83.3%) patients in group F, the sensory level showed regression to T12 within 180 minutes. However, 27 (90%) patients in group D and 5 (16.7%) patients in group F showed sensory regression to T12 after 180 minutes.

The mean time to achieve sensory regression to T12 level in group C (139.5 ± 13.60 min) was shorter as compared to group F (169.66 ± 13.76 min) and group D (208.116 ± 16.21 min) and these differences were found to be highly significant statistically ($p<0.001$). The difference in the results between group D and group F was statistically significant, with group D having a longer duration of sensory block. Thus, dexmedetomidine (Group D) has a longer duration of sensory block than bupivacaine (Group C) and fentanyl (Group F).

It was time taken from injection of the study drug to regression of motor block to Bromage grade 0 and noted in minutes. The mean duration of a complete motor block in group C was 179.16 ± 14.62 min, in group D it was 265.66 ± 19.24 min, and in group F it was 209.66 ± 14.73 min. The differences in mean duration of complete motor block between the three groups were found to be statistically highly significant ($p<0.001$). Group D showed a longer duration of complete motor block than groups C and F, while the duration of complete motor block in group F was longer than group C, both of

which were found to be statistically highly significant (p<0.001). Thus, dexmedetomidine (Group D) has a longer duration of complete motor block than bupivacaine (Group C) and fentanyl (Group F).

Time (min)	**Group C**	**Group D**	**Group F**
120-150	1 (3.3%)	0 (0%)	0 (0%)
150-180	12 (40%)	0 (0%)	0 (0%)
181-210	17 (56.7%)	0 (0%)	5 (16.7%)
211-240	0 (0%)	0 (0%)	17 (56.7%)
241-270	0 (0%)	6 (20%)	8 (26.7%)
271-300	0 (0%)	11 (36.7%)	0 (0%)
301-330	0 (0%)	11 (36.7%)	0 (0%)
331-360	0 (0%)	2 (6.7%)	0 (0%)
Total	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	187.5 ± 15.07 min	301 ± 25.77 min	234 ± 16.31 min
One way ANOVA	F= 253.06 , P<0.001, HS		
Multiple Comparison	**Group C vs. Group D**	**Group C vs. Group F**	**Group D vs. Group F**
p-value	<0.001, HS	<0.001, HS	<0.001, HS
P-value is significant if < 0.05 and highly significant if < 0.001.			
Table 2: Comparison of Duration of Complete Analgesia			

The total duration of complete analgesia was taken as the time between the administration of the local anaesthetic intrathecally and the onset of tolerable pain (VAS ≥ 0) at rest.
The mean duration of complete analgesia in group C was 187.5 ± 15.07 min; in group F, it was 234 ± 16.31 min; and in group D, it was 301 ± 25.77 min.
The differences in mean duration of complete analgesia between the three groups were found to be statistically highly significant (p<0.001). Group D showed a longer duration of complete analgesia than groups C and F, while the duration of analgesia in group F was longer than that in group C, both of which were found to be statistically highly significant (p<0.001). Thus, dexmedetomidine (Group D) has a longer duration of complete analgesia than bupativacaine (Group C) and fentanyl (Group F).

Time (min)	**Group C**	**Group D**	**Group F**
181-210	9 (30%)	0 (0%)	0 (0%)
211-240	15 (50%)	0 (0%)	1 (3.3%)
241-270	6 (20%)	0 (0%)	10 (33.3%)
271-300	0 (0%)	4 (13.3%)	15 (50%)
301-330	0 (0%)	5 (16.7%)	4 (13.3%)
331-360	0 (0%)	10 (33.3%)	0 (0%)
361-390	0 (0%)	8 (26.7%)	0 (0%)
391-420	0 (0%)	3 (10%)	0 (0%)
TOTAL	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	228.16 ± 17.54 min	358 ± 32.63 min	284.33 ± 20.45 min
One way ANOVA	F= 213.04 , P<0.001, HS		
Multiple Comparison	**Group C vs. Group D**	**Group C vs. Group F**	**Group D vs. Group F**
p-value	<0.001, HS	<0.001, HS	<0.001, HS
Comparison of time of rescue analgesia			
P-value is significant if < 0.05 and highly significant if < 0.001			
	Group C	**Group D**	**Group F**
MEAN ± SD	212.5 ± 28.42 mg	160 ± 38.05 mg	187.5 ± 38.14 mg
One way ANOVA	F= 16.72 , P<0.0001, HS		
Multiple Comparison	**Group C vs. Group D**	**Group C vs. Group F**	**Group D vs. Group F**
p-value	<0.001, HS	0.022, S	0.010, S
Comparison of Total Amount of Analgesia Required Post-Operatively			
P-value is significant if < 0.05 and highly significant if < 0.001			
Table 3			

The time of rescue analgesia was the time from intrathecal injection to a VAS score greater than or equal to 4 at rest, requiring supplementary (rescue) analgesia in the form of inj. diclofenac sodium intramuscular at a dosage of 1.5 mg/kg.

The mean time of rescue analgesia in group C was 228.16 ± 17.54 min, in group F it was 284.33 ± 20.45 min, and in group D it was 358 ± 32.63 min.

The differences in the mean time of rescue analgesia between the three groups were found to be statistically highly significant ($p<0.001$). Group D showed a longer duration of time for rescue analgesia than groups C and F, while the time for rescue analgesia in group F was longer than group C, both of which were found to be statistically highly significant ($p<0.001$). Thus, dexmedetomidine (Group D) has a longer duration of time for rescue analgesia than bupivacaine (Group C) and fentanyl (Group F).

VAS scores were used to assess the amount of analgesic required postoperatively. The VAS (Visual Analogue Scale) score was used intraoperatively and postoperatively at 0, 60, 120, 180, 240, 360, 480 minutes, 12 hours, and 24 hours. When the score was more than 4, injection diclofenac was given intramuscularly as a rescue analgesic at a dosage of 1.5 mg/kg.

The mean amount of analgesic required postoperatively in group C was 212.5 ± 28.42 mg, in group F it was 187.5 ± 38.14 mg, and in group D it was 160 ± 38.05 mg.

The differences in the mean amount of analgesic required postoperatively between the three groups were found to be statistically significant. Group D required a lesser amount of drug for analgesia than groups C and F, while the amount of analgesia required in group F was less than that in group C, both of which were found to be statistically significant. Thus, dexmedetomidine (Group D) required a lesser amount of analgesic drug as compared to bupivacaine (Group C) and fentanyl (Group F).

Time (min)	**Group C**	**Group D**	**Group F**	**p-value**
0	1.53 ± 1.96	1.46 ± 2.12	1.5 ± 2.17	
60	0	0	0	0.9924, NS
120	0	0	0	0.9924, NS
180	1 ± 1.20	0	0	0.1780,NS
240	1.6 ± 2.09	0	1.16 ± 1.08	0.0504, NS
360	0	2.56 ± 2.04	0	0.0001, HS
480	1.93 ± 0.25	0	0	0.00006, HS
12 hr	2.36 ± 0.49	1.56 ± 0.50	2.13 ± 0.34	0.3824, NS
24 hr	2.23 ± 0.43	1.66 ± 0.48	1.76 ± 0.50	0.6146, NS
Comparison of Mean Pain Scores at Various Time Intervals				
p-value is significant if < 0.05 and highly significant if < 0.001				
Time (min)	**Group C**	**Group D**	**Group F**	**p-value**
0	2	2	2	
15	2	2.03 ± 0.28	2	0.3721, NS
30	2	2.66 ± 0 .47	2.16 ± 0.37	<0.0001, HS
60	2.3 ± 0.46	3.16 ± 0.53	2.36 ± 0.49	<0.0001, HS
120	2.5 ± 0.50	3.1 ± 0.66	2.4 ± 0.49	<0.0001, HS
180	2	2.53 ± 0.50	2.46 ± 0.50	<0.0001, HS
240	2	2.46 ± 0.50	2.26 ± 0.44	0.0001, HS
360	2	2.2 ± 0.40	2	0.0012, HS
480	2	2	2	-
Comparison of Sedation Score Using Ramsay Sedation Scale				
p-value is significant if < 0.05 and highly significant if < 0.001				
Table 4				

VAS was assessed on a 10-cm scale, with 0 cm showing no pain and 10cm = worst pain. The mean VAS score between the three groups was comparable preoperatively and until 120 minutes after the injection of the spinal drug.

At 180 and 240 min, increasing VAS was seen in group C when compared with the other two groups, D and F, but it was statistically insignificant ($p > 0.05$). However, at 480 minutes, the VAS score in group C was raised to a statistically significant level as compared to groups D and F. This increase in VAS can be attributed to the shorter duration of analgesia of bupivacaine alone, which showed higher pain scores at 180, 240, and 480-minute intervals.

At 360 minutes, the VAS score in group D was higher as compared to both groups C and F, which was found to be statistically significant. At 12 and 24 hours postoperatively, the VAS score among the three groups was found to be comparable. The quality of analgesia was assessed subjectively by the VAS, and the comparable mean VAS shows good quality of analgesia in between the three groups.

The mean sedation scores were found to be comparable and statistically insignificant ($p > 0.05$) preoperatively and at 15 minutes among the three groups. But it was found that the sedation score was higher in group D as compared to both groups C and F at 30, 60, 120, 240, and 360 minute intervals, which was found to be statistically significant ($p<0.001$).

The maximum number of patients in the three groups exhibited a score of two or more at all the time intervals. Intraoperative sedation in any form was avoided to minimize interference during the assessment of the blockade characteristics.

DISCUSSION

Time of Regression to T12

27 (90%) patients in group D and 5 (16.7%) patients in group F showed sensory regression to T12 after 180 minutes. Iheb Labbene et al.[2] in their study of comparison between different doses of hyperbaric bupivacaine (5, 7.5, or 10 mg) with 25 µg of fentanyl reported that time to T12 regression was prolonged in a dose-dependent manner. The time to regression to T12 in patients induced with fentanyl has not been mentioned by most of the authors. However, our study shows a longer time to regression to T12 in the fentanyl group as compared to the above studies. This might be attributed to the higher dosage of bupivacaine used in our study.

The time to regression to T12 when dexmedetomidine is administered along with bupivacaine intrathecally has not been commented on by any authors. However, many authors have mentioned significantly prolonged time to regression to S1 or S2 with addition of dexmedetomidine with the bupivacaine compared to bupivacaine with fentanyl or bupivacaine alone.

Total Duration of Motor Blockade

The differences in mean duration of complete motor block between the three groups were found to be statistically highly significant ($p<0.001$). Group D showed a longer duration of complete motor block than groups C and F, while the duration of complete motor block in group F was longer than group C, both of which were found to be statistically highly significant ($p<0.001$). Thus, dexmedetomidine (Group D) has a longer duration of complete motor block than bupivacaine (Group C) and fentanyl (Group F). Rajni Gupta et al.[3] stated that the duration of complete motor block was significantly longer in the dexmedetomidine group (421 ± 21 min) than in the fentanyl group (149.3 ± 18.2 min) in their study. Al-Ghanem et al.[4] in their study that the duration of complete motor block was significantly longer in the dexmedetomidine group (240 ± 64 min) than in the fentanyl group (155 ± 46 min). M. Mustafa et al.[5] and Hala et al.[6] in their study that the duration of complete motor block was significantly prolonged with dexmedetomidine as compared to bupivacaine.

The results of the above-mentioned studies corroborate our study, as it shows that the duration of complete motor block was significantly longer in the dexmedetomidine group than in the fentanyl and bupivacaine groups. While at the same time, the duration of motor block in the fentanyl group was significantly longer than in the bupivacaine group.

Total Duration of Complete Analgesia

The differences in mean duration of analgesia between the three groups were found to be statistically highly significant ($p<0.001$). Group D showed a longer duration of analgesia than groups C and F,

while the duration of analgesia in group F was longer than group C, both of which were found to be statistically highly significant ($p<0.001$).

Yegin et al.[7] in their study reported that the time to first feeling of pain, i.e., duration of analgesia was 150 ± 33 min in the fentanyl group as compared to 120 ± 32 min in the ropivacaine group, which was statistically significant. The above studies show that fentanyl has a significantly longer duration of analgesia as compared to bupivacaine, so our study correlates with the above studies. Though there are studies in the literature on the beneficial effects of the addition of intrathecal dexmedetomidine to hyperbaric bupivacaine on prolonged postoperative analgesia, its influence on the duration of complete analgesia has not been commented on in most studies.

Time of Rescue Analgesia

The differences in the mean time of rescue analgesia between the three groups were found to be statistically highly significant ($p<0.001$). Group D showed a longer duration of time for rescue analgesia than groups C and F, while the time for rescue analgesia in group F was longer than that in group C, both of which were found to be statistically highly significant ($p<0.001$). Yegin et al. in their study, reported that the time to first rescue analgesia was 210 ± 31 min in the fentanyl group as compared to 180 ± 26 min in the ropivacaine group ($p<0.05$).

P. Motiani et al.[8] stated that the duration of effective analgesia, i.e., the time of rescue analgesia was 485.1 ± 82.7 min in the fentanyl group as compared to 256.3 ± 60.2 min in the bupivacaine group, which was statistically significant.

Comparison of Total Amount of Analgesia Required Postoperatively

The differences in the mean amount of analgesic required postoperatively between the three groups were found to be statistically significant. Group D required a lesser amount of drug for analgesia than groups C and F, while the amount of analgesia required in group F was less than that in group C, both of which were found to be statistically significant. A study conducted by Rajni Gupta et al. stated that the total analgesic dose of diclofenac required in 24 hours was significantly lower in dexmedetomidine (80 ± 67 mg) as compared to fentanyl (180 ± 70 mg) in their study.

Quality of Anaesthesia and Analgesia

The comparable mean VAS score shows a good quality of analgesia between the three groups. The overall 24-hour VAS score was lower for dexmedetomidine with prolonged postoperative analgesia as compared to fentanyl and bupivacaine. Amit Jain et al., in their study, showed that the overall 24-hour VAS score was significantly lower with fentanyl (4.3 ± 0.7) as compared to hyperbaric bupivacaine (4.9 ± 0.6). P. Motiani et al. and Marzieh et al.[9] in their studies that the overall VAS score was reduced in fentanyl as compared to bupivacaine with improved quality of analgesia. Thus, our study findings correlate with the results of the above studies.

Sedation Score

This was judged subjectively to assess the degree of sedation produced in the patient and evaluated preoperatively and intraoperatively at regular intervals of 0, 15, 30, 60, 120, 180, 240, 360, and 480 min according to the Ramsay Sedation Scale.

The mean sedation scores were found to be comparable and statistically insignificant ($p > 0.05$) preoperatively and at 15 minutes among the three groups. But it was found that the sedation score was higher in group D as compared to both groups C and F at 30, 60, 120, 240, and 360 minute intervals, which was found to be statistically significant ($p<0.001$).

The maximum number of patients in the three groups exhibited a score of two or more at all the time intervals. Intraoperative sedation in any form was avoided to minimise interference during the assessment of the blockade characteristics.

A α2 agonists produce a sedative effect by acting on α 2-adrenergic receptors in locus ceruleus. The sedation that happens after dexmedetomidine is injected into the skull may be because it is absorbed by the body and moved through the bloodstream to higher centres or moved cephalad in the cerebrospinal fluid.

Rajni Gupta et al. reported in their study that the mean sedation score was higher in dexmedetomidine (3.8 ± 0.5) as compared to 2.2 ± 0.53 in fentanyl, which was statistically significant. But a study conducted by Kanazi et al.[10] to compare dexmedetomidine, clonidine, and hyperbaric bupivacaine stated that the sedation scores were in the range 0–1 in all three groups.

Monitoring of Vitals

Vital parameters (like pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, respiratory rate and SpO2) of the patient were monitored every 2 minute interval for the first 10 minutes, then every 5 minute interval till 30 minutes, every 15 minute interval till 60 minutes, every 30 minute till 120 minutes, every hour till 4 hours and then every 2 hours up to 8 hours.

CONCLUSION

Both dexmedetomidine and fentanyl had a comparably faster onset of sensory and motor blockade as compared to 0.5% bupivacaine. Dexmedetomidine significantly prolonged the duration of sensory and motor block with excellent quality of anesthesia as compared to fentanyl and bupivacaine. Dexmedetomidine as an adjuvant significantly prolongs the duration of complete analgesia and the time of rescue analgesia as compared to fentanyl and bupivacaine. The postoperative analgesic requirement was less for dexmedetomidine as compared to fentanyl and bupivacaine, leading to improved quality of analgesia. Hemodynamic alterations in the three groups were found to be minimal. No unexpected adverse events were registered. The adverse effects that occurred in the three groups were statistically insignificant.

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