



A COMPARITIVE STUDY OF INTRATHECAL FENTANYL AND DEXMEDETOMIDINE AS ADJUVIANTS TO BUPIVACAINE

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ABSTRACT

Aim of the Study: To study the efficacy of Intrathecal Fentanyl and Dexmedetomidine with Bupivacaine for infra umbilical surgeries. **Material & Methods:** A prospective randomized double blinded comparative study has been conducted in 100 patients belonging to ASA physical status I & II of both sexes were divided into two groups of 50 each. **Results:** Time from injection to highest sensory level and Onset of Bromage 3 was similar in both groups. Time from injection to T10 sensory level was significantly shorter in Group D ($p < 0.001$), and Time for regression to Bromage 0 was significantly longer in group D ($p < 0.001$). Intraoperatively both groups remained haemodynamically stable. Incidence of bradycardia was more in Group D and incidence of pruritus was more in Group F though it was not statistically significant ($p = 0.402$). Intraoperative sedation was higher in Group D ($p < 0.001$) and post operatively Visual analogue scores were significantly lower with group D ($p < 0.001$). **Conclusion:** Dexmedetomidine appears to be an attractive adjuvant to intrathecal bupivacaine than Fentanyl as there is significantly longer duration of motor block, additional benefits of intraoperative sedation and decreased analgesic requirement in the post-operative period.

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INTRODUCTION

Spinal anaesthesia is the most preferred regional anaesthesia technique as it is easy to perform, economical and produces rapid onset of anaesthesia and complete muscle relaxation. The aim of intrathecal local anaesthetic is to provide adequate sensory and motor block necessary for all infra umbilical surgeries. Hyperbaric bupivacaine is the most commonly used intrathecal local anaesthetic¹.

Various adjuvants have been added to bupivacaine to shorten the onset of block and prolong the duration of block. Fentanyl, a lipophilic opioid agonist, is used as an adjuvant, which prolongs the duration of spinal block. Dexmedetomidine, an α -2 agonist drug, when given intrathecal space, significantly prolongs the duration of spinal block².

Therefore, the present study was performed to compare the efficacy of Fentanyl and Dexmedetomidine as adjuvants to sub arachnoid block.

Aim of the Study

The aim of the study is to compare the following factors in two groups:

1. Hyperbaric bupivacaine 0.5% and 25 μ gm Fentanyl

2. Hyperbaric bupivacaine 0.5% and 5 μ gm Dexmedetomidine when given intrathecally

MATERIAL & METHODS

Inpatients, posted for major surgeries, below umbilical level, in Osmania General Hospital were chosen for the study from November 2019 to October 2021.

Inclusion Criteria

- ASA physical status class I and II
- Age between 18 – 65 years of either sex.

Exclusion Criteria

- Emergency surgery
- Deformities of the spine
- Hypersensitivity to any of the drugs in the study
- Contraindications to spinal Anaesthesia – patient refusal, bleeding diathesis

METHODOLOGY

- After approval from the ethical committee of our college, 100 ASA I and II patients scheduled for major surgeries under spinal anaesthesia were chosen for the study

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- Pre anaesthetic check-up was done one day prior to the surgery. Patients were evaluated for any systemic diseases and laboratory investigations recorded. The procedure of SAB was explained to the patients and written consent was obtained. The patients were educated about the use of visual analogue scale.
- Preparation of patients included period of overnight fasting.
- Patients were pre medicated with Tab. Rantac 150 mg and Tab. Anxit 0.5 mg H.S.

Preparation of Operating Theatre

- Boyle’s anaesthesia machine was checked. Appropriate size endotracheal tubes, working laryngoscope with medium and large size blades, stylet and working suction apparatus were kept ready before the procedure.
- Emergency drug tray consisting of atropine, adrenaline, mephenteramine, ephedrine and dopamine were kept ready.

Procedure

- Patients shifted to OR table, IV access was obtained on the forearm with No 18G IV cannula and all patients were preloaded with 15 ml / Kg, Ringer’s Lactate, 15 mins before the surgery.
- Patients were randomly allocated into two groups
- Baseline vitals were recorded.
- Under strict asepsis, using 25 G Quincke spinal needle, lumbar puncture was performed at L 3 – L 4 space
- Group F received 3ml , 0.5 % hyperbaric bupivacaine + 25 µg Fentanyl (vol 0.5ml)
- Group D received 3ml, 0.5 % hyperbaric bupivacaine + 5 µg Dexmedetomidine (vol 0.5 ml)
- Intraoperatively pulse rate, non-invasive blood pressure, electrocardiogram, SpO2 was recorded, every 2 minutes for the first 10 minutes, every 10 minutes for the next 50 minutes and every 15 minutes till the end of surgery
- Time of onset of T10 sensory block and peak sensory block was noted using pin prick method, time of onset of Bromage 3 motor block was noted.

Motor block was assessed with Modified Bromage scale

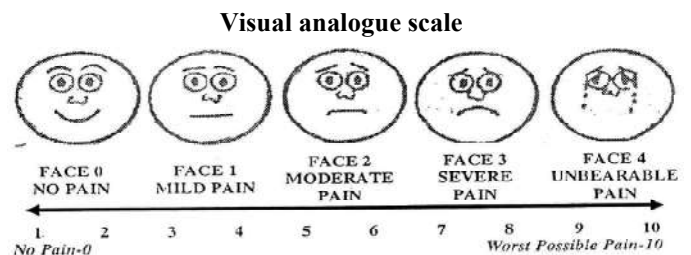
- Bromage 0 - the patient is able to move the hip, knee and ankle
- Bromage 1 - the patient is unable to move the hip but is able to move the knee and Ankle
- Bromage 2 - the patient is unable to move the hip and knee but able to move the ankle
- Bromage 3 - the patient is unable to move the hip, knee and ankle

Modified Ramsay sedation scale was used for intraoperative sedation

1. agitated, restless
2. cooperative, tranquil
3. responds to verbal commands while sleeping
4. brisk response to glabellar tap or loud noise while sleeping
5. sluggish response to glabellar tap or loud noise while sleeping
6. no response to glabellar tap or loud noise while sleeping

Following parameters were recorded

- Hypotension (> 20 % fall of baseline blood pressure) was treated with bolus dose of 6 mg mephenteramine i.v.
 - Bradycardia (pulse rate < 50 bpm), was treated with 0.6 mg atropine i.v.
 - Incidence of respiratory depression defined as respiratory rate less than 9 /min and SpO2 less than 90 % on room air, was noted.
 - Side effects if any were noted.
 - Post operatively regression of the sensory block and the motor blockade to reach modified Bromage 0 was noted.
 - Pain was assessed using “Visual Analogue Scale” advocated by Reville and Robinson in 1976. It is linear scale, consists of 10 cm line anchored at one end by a label such as “No pain” and other end by “Worst pain imaginable”. Patient simply marks the line to indicate the pain intensity. Supplemental analgesia was given for visual analogue score of more than 6. Time of supplemental analgesia was noted.
 - Visual analogue scale was used to assess post-operative pain.
- 0 = no pain, 10 = severe pain.



Drug Tray



Statistical Methods 3, 4, 5, 6

Statistical Methods: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made.

Assumption: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, and Cases of the samples should be independent.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups

Study Design: A Comparative two group randomized clinical study with 100 patients with 50 patients in Group F(Fentanyl) and 50 patients in Group D (Dexmedetomidine) is undertaken to study the changes in haemodynamics and side effects. Statistical analysis was done by applying Chi-square test, Anova test and student's 't' test to analyse the data, p value was determined.

P > 0.05 is not significant.

P < 0.05 is significant.

P < 0.001 is highly significant.

RESULTS

The patients who took part in this project were in the age group of 18 to 65 years. On statistical comparison the two groups were comparable in age distribution.

Table 1 Surgery in two groups of patients studied

Surgery	Group F (n=50)		Group D (n= 50)	
	No	%	No	%
Vaginal hysterectomy	10	20.0	11	22.0
Abdominal hysterectomy	8	16.0	1	2.0
ORIF	7	14.0	10	20.0
TURP	3	6.0	1	2.0
URS	2	4.0	3	6.0
Mesh repair	3	6.0	1	2.0
Below Knee Procedure	2	4.0	3	6.0
Stripping and ligation	3	6.0	1	2.0
Tension band wiring	2	4.0	1	2.0
Implant removal	0	0.0	2	4.0
Intervalappendicectomy	0	0.0	2	4.0
Fistula repair	0	0.0	1	2.0
Screw fixation	0	0.0	1	2.0
Skin grafting	0	0.0	1	2.0
Internal urethrotomy	1	2.0	1	2.0
DHS	1	2.0	0	0.0
Others	8	16.0	10	20.0

Table 2 Comparison of time of injection to T10, Highest sensory level, onset of Bromage 3 and regression to Bromage 0

Variables	Group F	Group D	P value
Time from injection to T10 (minutes)	3.38 ± 0.83	2.62 ± 0.56	< 0.001
Time from injection to highest sensory level (minutes)	11.47 ± 1.23	11.72 ± 1.23	0.314
Onset of Bromage 3 (minutes)	10.38 ± 1.08	10.59 ± 1.00	0.317
Regression to bromage 0 (minutes)	152.90 ± 8.31	419.70 ± 16.85	< 0.001

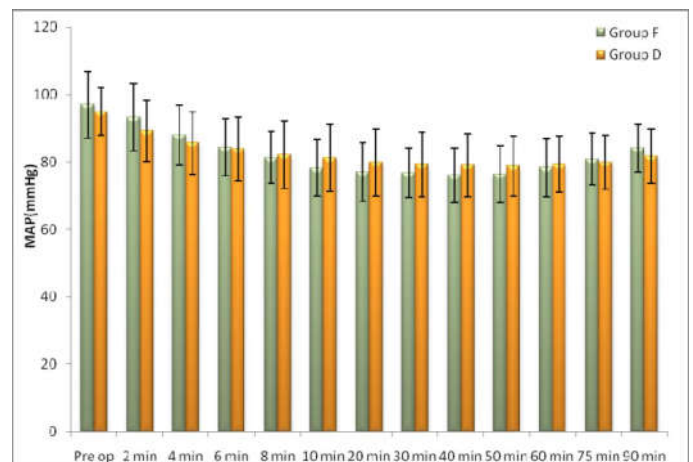
Table 3 Comparison of Systolic Blood pressure (mm Hg) in two groups of patients studied

SBP (mmHg)	Group F	Group D	P value
Pre OP	128.60 ± 11.70	126.20 ± 9.54	0.264
2 minutes	125.12 ± 12.11	119.40 ± 10.65	0.014
4 minutes	119.10 ± 11.34	114.84 ± 10.85	0.058
6 minutes	115.24 ± 9.77	112.76 ± 10.84	0.233
8 minutes	112.42 ± 9.04	110.92 ± 10.86	0.455
10 minutes	110.22 ± 9.87	110.50 ± 10.50	0.891
20 minutes	109.46 ± 9.70	109.38 ± 10.77	0.969
30 minutes	107.66 ± 9.98	108.34 ± 10.57	0.736
40 minutes	106.64 ± 9.98	107.32 ± 10.20	0.737
50 minutes	108.82 ± 10.18	107.12 ± 9.75	0.881

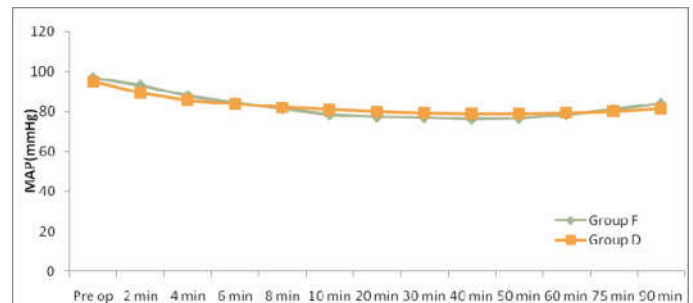
60 minutes	108.98 ± 9.74	107.82 ± 9.20	0.542
75 minutes	111.24 ± 9.57	108.60 ± 8.88	0.156
90 minutes	114.58 ± 8.32	110.56 ± 8.55	0.019

Table 4 Comparison of Diastolic Blood pressure (mm Hg) in two groups of patients studied

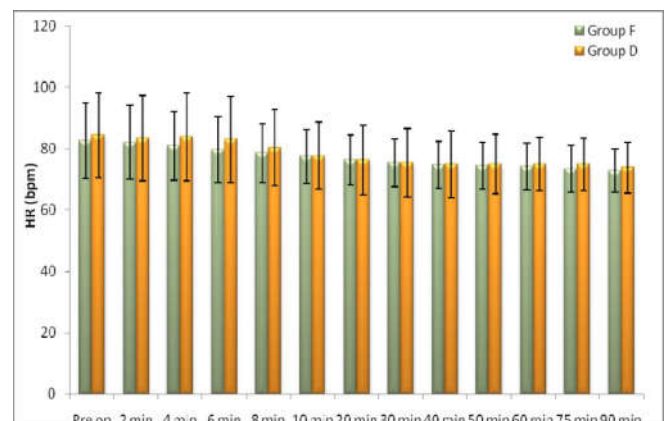
SBP (mmHg)	Group F	Group D	P value
Pre OP	80.10 ± 8.58	80.78 ± 7.81	0.679
2 minutes	77.38 ± 9.63	74.18 ± 9.22	0.094
4 minutes	72.46 ± 8.56	71.06 ± 9.48	0.440
6 minutes	69.04 ± 8.65	69.44 ± 9.56	0.827
8 minutes	65.76 ± 7.87	67.74 ± 10.31	0.283
10 minutes	62.30 ± 8.39	66.68 ± 10.31	0.022
20 minutes	60.92 ± 9.23	65.12 ± 9.96	0.031
30 minutes	61.36 ± 7.40	64.80 ± 9.66	0.048
40 minutes	60.90 ± 8.25	64.94 ± 9.62	0.026
50 minutes	61.28 ± 8.50	64.76 ± 9.28	0.053
60 minutes	62.98 ± 8.79	65.16 ± 8.90	0.221
75 minutes	65.75 ± 7.53	65.62 ± 8.30	0.933
90 minutes	69.00 ± 7.54	67.18 ± 8.42	0.258



Graph 1 Comparison of MAP (mm Hg) in two groups of patients studied



Graph 2 Comparison of Heart Rate (beats per minutes) in two groups of patients studied



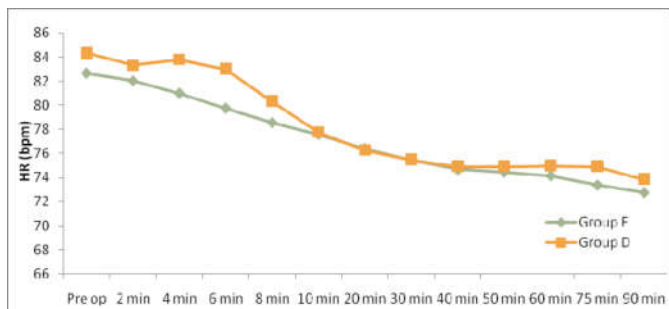
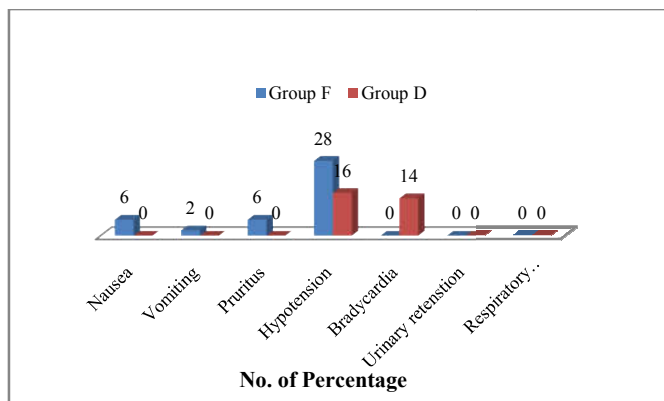


Table 5 Comparison of RR and SPO2 of two groups

Variables	Group F	Group D	P value
Respiratory rate (RR)	16.10 ± 1.61	16.10 ± 1.61	1.000
SPO2	97.92 ± 0.75	97.92 ± 0.75	1.000



Graph 3 Side Effects of patients in two groups studied

DISCUSSION

Spinal anaesthesia is the most preferred regional anaesthesia technique as it is easy to perform, produces rapid onset of anaesthesia and complete muscle relaxation and is also economical. These advantages are sometimes offset by a relatively short duration of action.

The aim of intrathecal local anaesthetic is to provide adequate sensory and motor block necessary for all infra umbilical surgeries. Hyperbaric bupivacaine is the most commonly used intrathecal local anaesthetic. Various adjuvants have been added to bupivacaine to shorten the onset of block and prolong the duration of block.

Fentanyl, a lipophilic opioid agonist, is used as an adjuvant, which prolongs the duration of spinal anaesthesia. Fentanyl is a lipophilic μ -receptor agonist opioid. Intrathecally, Fentanyl exerts its effect by combining with opioid receptors in the dorsal horn of spinal cord and may have a supraspinal spread and action⁷

Dexmedetomidine, an α -2 agonist drug, when given intrathecally, significantly prolongs the duration of spinal anaesthesia. Intrathecal α -2 receptor agonists have been found to have antinociceptive action for both somatic and visceral pain⁸

Therefore, the present study was performed to compare Fentanyl and Dexmedetomidine in their efficacy as adjuvants to spinal anaesthesia. In our study, the intrathecal dose of Dexmedetomidine selected was based on previous animal studies. A number of animal studies conducted using intrathecal Dexmedetomidine at a dose range of 2.5-100 μ g did not report any neurologic deficits with its use.

In our study design Group F received 0.5% of hyperbaric Bupivacaine 3ml with Fentanyl 25 μ g and Group D received 0.5% hyperbaric Bupivacaine 3ml with Dexmedetomidine 5 μ g, injected intrathecally to the patients undergoing infra-umbilical surgeries.

The following parameters were observed

- Time of onset of action
- Highest level of sensory and motor blockade
- Time of onset of Bromage 0
- Intraoperative heart rate, Blood pressure, SpO2
- Intraoperative sedation
- Regression to Bromage 3
- Post-operative requirement of analgesia

Kanazi et al⁹ found that 3 μ g Dexmedetomidine or 30 μ g clonidine added to 13 mg spinal bupivacaine produced the same duration of sensory and motor block with minimal side effects in urologic surgical patients. From Kanazi study and animal studies, we assumed that 3-5 μ g Dexmedetomidine would be equipotent to 30-45 μ g clonidine when used for supplementation of spinal bupivacaine.

Our study has shown that the addition of 5 μ g Dexmedetomidine with hyperbaric bupivacaine significantly prolongs both sensory and motor block. Both Fentanyl and Dexmedetomidine provided good quality intraoperative analgesia. The analgesia was clinically better in group D as compared to group F. Small doses of intrathecal Dexmedetomidine (3 μ g) used in combination with bupivacaine in humans have been shown to shorten the onset of motor block and prolong the duration of motor and sensory block with hemodynamic stability and lack of sedation.

Al-Ghanem et al¹⁰ had studied the effect of addition of 5 μ g Dexmedetomidine or 25 μ g Fentanyl intrathecal to 10 mg isobaric bupivacaine in vaginal hysterectomy and concluded that 5 μ g Dexmedetomidine produces more prolonged motor and sensory block as compared with 25 μ g Fentanyl.

In our study, in the Dexmedetomidine group we found longer duration of both sensory and motor blockade and good patient satisfaction.

Al-Mustafa et al¹¹ studied effect of Dexmedetomidine 5 μ g and 10 μ g with bupivacaine in urological procedures and found that Dexmedetomidine prolongs the duration of spinal anaesthesia in a dose-dependent manner. Visceral pain usually occurs during abdominal surgery under spinal anaesthesia. Intrathecal Fentanyl when added to local anaesthetics reduces visceral and somatic pain. In our study also no patient perceived visceral pain in both D and F groups.

Rajni Gupta, Reetu Verma, Jaishri Bogra et al¹² (2011) used Dexmedetomidine as an intrathecal adjuvant for post-operative analgesia and found that the addition of 5 μ g Dexmedetomidine to ropivacaine intrathecally produces prolongation in the duration of motor and sensory block. They also found that intraoperative ephedrine requirement was more in group D as compared to group R. In our study intraoperative incidence of hypotension was higher in group F.

Rajni Gupta, Reetu Verma, Jaishri Bogra et al¹³ conducted a comparative study of intrathecal Dexmedetomidine 5 μ gm and Fentanyl 25 μ gm as adjuvants to bupivacaine and found that intrathecal Dexmedetomidine is associated with prolonged

motor and sensory block, hemodynamic stability, and reduced demand for rescue analgesics in 24 hrs as compared to Fentanyl. In our study also the post-operative analgesic requirements were significantly less in the Dexmedetomidine group than group Fentanyl. They also found that the sedation score was more in group D patients. The mean sedation score was 3.8 ± 0.5 in group D as compared to 2.2 ± 0.53 in group F, which was statistically significant ($P < 0.05$). In our study the mean sedation score for group F was 2.16 ± 0.37 and group D was 3.40 ± 0.49 , which was statistically significant ($p < 0.001$). There was no incidence of respiratory depression.

Pruritus after intrathecal Fentanyl is known but it was not significant in the present study. The α -2 adrenergic agents also have anti-shivering property as observed by *Talke et al*¹⁴ and *Maroof M et al*¹⁵. We too did not find any incidence of shivering.

CONCLUSION

- Addition of 5 μ g Dexmedetomidine with hyperbaric bupivacaine significantly prolongs both sensory and motor block.
- Intraoperatively, there was less incidence of side effects with Intrathecal Dexmedetomidine when compared to Intrathecal fentanyl.
- The post-operative 24 hours analgesic requirements were significantly less in the Dexmedetomidine group than group Fentanyl.
- To conclude, 5 μ g Dexmedetomidine seems to be an attractive alternative to 25 μ g Fentanyl as an adjuvant to spinal bupivacaine in surgical procedures. It provides good quality of intraoperative analgesia, haemodynamically stable conditions, minimal side effects, and excellent quality of postoperative analgesia.

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