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A Comparative Study of Intrathecal 12.5 Mg 0.5% Hyperbaric Bupivacaine + 5 µg Dexmedetomidine VS 12.5 Mg 0.5% HyperbaricBupivacaine + 25 µg FENTANYL

Dr.M.Santhi Sree[1], Dr.A. Usha Rani [2],Dr.Shanthi Jagan Sushma
1st Author- Associate Professor, Department of Anaesthesia, SMC,V ijayawada,
,2nd Corresponding Author- Assistant Professor, Department of Anaesthesia, SMC,V ijayawada,
3 r d Author-Senior resident, , Department of Anaesthesia SMC,Vijayawada

Abstract:
Background and Aims: *The objective is to compare the efficacy of addition of dexmedetomidine or fentanyl to bupivacaine in sensory and motor blockade duration, two segment regression and time of first analgesic requirement. Use of low-dose spinal anaesthesia is advantageous in elderly as it reduces the hemodynamic and heart rate variability.* ***Methods:*** *sixty patients are randomly allocated into two Group F: received 12.5 mg of 0.5% hyperbaric bupivacaine along with 25mcg fentanyl; Group D: received 12.5 mg of 0.5% hyperbaric bupivacaine along with 5 mcg of dexmedetomidine. Data between the 2 groups were compared and analysed using ANOVA test and chi square test.* ***Results****: All 60patients completed the study. Mean duration of analgesia was 201.16±8.49 (Group F), 303±35.38 min (Group D) , .Time to complete motor recovery was 188min (Group F) and 367 min (Group D) and 239+/-61.71min (Group F).* ***Conclusion:*** *Addition of fentanyl (25µg) or dexmedetomidine (5 µg) to intrathecal bupivacaine for lower abdominal surgery prolongs the time to the first analgesic request*

Keywords: *Anaesthesia, fentanyl, dexmedetomidine, intrathecal.*

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I. Introduction

Spinal anesthesia is the most commonly used procedure for lower abdominal surgeries. Postoperative pain control is a significant problem because spinal anesthesia using onlylocal anesthetics is associated with less duration of action. Thus early analgesic intervention is required in the postoperative period. Common problems while performing lower abdominal surgeries under spinal anesthesia are nausea, visceral pain, vomiting. A number of adjuvants, such as opioids (Morphine, Fentanyl) and non-opioids such as α_2 agonist (Dexmedetomidine and clonidine) and others midazolam, steroids have been studied to prolong the effects of spinal anesthesia.

Fentanyl, a lipophilic opioid, has a rapid onset of action. After intrathecal administration, Fentanyl diffuses into epidural space and subsequently into plasma, suggesting that it acts not only through spinal opioid receptors but also systemically. Adding Fentanyl to hyperbaric Bupivacaine improves the quality of intraoperative and early postoperative subarachnoid block than intrathecal Bupivacaine alone.

Dexmedetomidine is a highly selective α_2 adrenoreceptor agonist recently introduced to anesthesia practice. The highly lipophilic nature of Dexmedetomidine allows rapid absorption in cerebrospinal fluid and binding to the α_2 adrenoreceptor of the spinal cord for its analgesic action. It prolongs the duration of both sensory and motor blockade induced by local anesthetics.

II. Aims And Objectives

The study aims to compare the following factors in two groups, i.e.,

a) 12.5mg of 0.5% Hyperbaric Bupivacaine and 25µg fentanyl intrathecally.
b) 12.5mg of 0.5% Hyperbaric Bupivacaine and 5µg Dexmedetomidine intrathecally.

1. Onset and duration of sensory blockade :

Speed of onset as determined by lack of appreciation of pin-prick and analgesiaduration as determined by regression to S1 segment.

2. Onset and duration of motor blockade :

Speed of onset and duration of the motor blockade was assessed by Bromage scale.3.Intraoperative Hemodynamic changes :

Intraoperative hemodynamic changes are assessed by pulse rate and blood pressure.4.Side effects such as nausea, vomiting, hypotension, shivering, pruritis.

PATIENTS AND METHODS

After obtaining clinical approval from Institutional Ethical Committee and informed written consent, 60 patients of ASA physical class I and II who were posted for elective lower abdominal and lower limb surgeries at GGH Vijayawada were selected for the study.

The present prospective randomized double blinded clinical study was conducted from JANUARY 2019 to JUNE 2020.

Group D: Received 12.5mg (2.5ml) of 0.5% hyperbaric Bupivacaine with 5µg of

Dexmedetomidine intrathecally.

Group F: received 12.5mg (2.5ml) of 0.5% hyperbaric Bupivacaine with 25µg Fentanyl

intrathecally.

INCLUSION CRITERIA

60 patients of ASA physical grades I & II

Patients of either sex aged 20-50 years posted for lower abdominal and lower limbsurgeries

EXCLUSION CRITERIA

patient refusal

patient on adrenoreceptor agonists and antagonistspatient with cardiovascular comorbidities
patient allergic to study drugspatient with ASA grade 3 & 4 patients with obesity.

Methods of collection of data

Data were collected from 60 patients in the age group of 20-50 years of ASA class I & II, posted for lower abdominal and lower limb surgeries without any co-morbid diseases were grouped randomly. The study drug was prepared by an anesthesiologist, who was not included in the study. All spinal blocks were given by the same anesthesiologist,who was also an observer. Hence the patient and the observer were blinded for the study drug.

- Preoperative assessment was done for each patient on the night before the surgery

And written informed consent was taken.

- Patients were kept Nil per Oral for solids 6hrs and clear fluids 2hrs before surgery.
- Patients were pre-medicated on the night before surgery with the tablet Alprazolam 0.5mg.
- Patients were not pre-medicated on the day of surgery.
- Intravenous line was obtained with 18G cannula.
- Patients were connected to a multi-channel monitor for continuous monitoring of pulse rate (PR), arterial oxygen saturation (SpO2), electrocardiograph (ECG), non-invasive blood pressure (NIBP), and mean arterial pressure (MAP).
- Patients were positioned in flexed lateral position.
- under aseptic precautions, subarachnoid blocks were performed at L2-L3/L3- L4 inter- space through a midline approach using 25G Quincke's spinal needle after confirming the clear and free flow of CSF and the study drug was injected into the subarachnoid space. Patients were turned to supine posture immediately with the table kept flat and supplemental oxygen was given.

The following parameters were noted.

- Onset of the sensory blockade and motor blockade.
- Maximum level of sensory blockade attained and time taken for the same.

- Time for two segments sensory regression.
- Maximum level of motor blockade attained and the time taken for the same.
- Total duration of the sensory blockade and motor blockade
- Total duration of analgesia
- Sensory blockade was tested using the pinprick method with a 27G hypodermic needle at every 30 seconds for the first 2 minutes, every minute for the next 5 minutes and every 5 minutes for the next 15 minutes, and every 10 minutes for the next 30 minutes and every 15 minutes till the end of surgery and thereafter every 30 minutes until the sensory block is resolved.
- The motor blockade was assessed according to the Modified Bromage scale.
- All the patients were monitored during the period of a block and peri-operative period employing a multi-channel monitor which displays Heart rate, Systolic and Diastolic blood pressure, mean arterial pressure, ECG, SpO2.
- In the postoperative period, patients were monitored for postoperative pain by VAS scale (0 - 10) initially every hour for 2 hours, then every 2 hours for the next 8 hours,then every 4hr till 24hr, which was explained to the patients preoperatively.

When the VAS was,>4 patients were given rescue analgesia with Inj. Diclofenac75mg intramuscularly.

III. Observations & Results

The study population consists of 60 patients (20-50 years) posted for lower abdominaland lower limb surgeries.. They were divided into two groups 30 in each group.

Group-D-received 0.5% hyperbaric Bupivcaine 12.5mg (2.5ml) + 5µg Dexmedetomidine

Group-F -received 0.5% hyperbaric Bupivacaine 12.5mg (2.5ml) + 25µg Fentanyl

The following observations were made during the study.

Table 1: Mean time taken for sensory onset in minutes

Time taken for sensory onset in minutes	Group-D	Group-F	P value FvsD
Mean±SD	1.73±0.450	1.07±0.254	0.000
Minimum	1	1	
Maximum	2	2	

The mean time of onset of sensory blockade at T 10 in Group-D was 1.73±0.450mins and Group-F was 1.07±0.254mins. Statistically there was highly significant difference when Group-D was compared with Group-F (P<0.05).

Table 2: Maximum level of sensory block attained

Maximum level of sensory block attained	Groups				
	Group-D		Group-F		P value FvsD
	No	%	No	%	0.052
T4	27	90%	25	83.3%	
T6	3	10%	5	16.7%	
Total	30	100%	30	100%	

. 27 out of 30 patients in Group D and 25 out of 30 in Group-F had T4 level of sensory blockade
3 out of 30 in Group-D and 5 out of 30 in Group-F had T6 level of blockade

Statistically there was no significant difference when Group D was compared with Group F (P=0.052).

Table 3: Mean time taken for maximum sensory blockade in minutes

Mean time taken formaximum sensory blockade in minutes	Group-D	Group-F	P value FvsD
Mean±SD	9.86±0.89	10.13±0.73	0.387
Minimum	8	8	
Maximum	12	12	

. The mean time taken for maximum sensory blockade in Group-D was 9.86±0.89mins and Group-F was 10.13±0.73mins. Statistically there was no difference when Group-D was comparedwith Group-F (P=0.387).

Table 4: Mean time taken for regression of sensory block by two segments

Regression of sensory block by two segments inminutes	Group-D	Group-F	P value FvsD
Mean±SD	137.93±11.5	102.66±8.66	0.000
Minimum	120	90	
Maximum	158	122	

The mean time taken for regression of sensory block by two segments in Group-D was 137.93±11.5min and Group-F was 102.66±8.66min. Statistically there washighly significant difference when Group-F was compared with Group-D (P<

Table 5: Mean duration of analgesia in minutes

Duration of analgesia in minutes	Group-D	Group-F	P value FvsD
Mean±SD	303.33±35.38	201.16±8.49	0.000
Minimum	240	185	
Maximum	360	215	

. The mean duration of analgesia in Group-D was 303.33±35.38min and in Group-F was 201.16±8.49min. Statistically there was a highly significant difference between Group-F and Group- D($p<0.05$).

Table 6: Mean duration of sensory regression to S1 in minutes

Mean duration of sensory regression to S1	Group-D	Group-F	P value FvsD
Mean±SD	396.80±30.87	226.50±13.62	0.000
Minimum	335	202	
Maximum	445	250	

Table 7: Time taken for onset of motor blockade in minutes

Mean time taken for onset of motor blockade	Group-D	Group-F	P value FvsD
Mean±SD	1.10±0.30	1.03±18	0.309
Minimum	1	1	
Maximum	2	2	

The mean time taken for onset of motor blockade in Group-D was 1.10±0.30min and Group-F was 1.03±18min. Statistically there was no difference when Group-F wascompared with Group-D (P=0.309).

Table 8: Mean time taken for maximum motor blockade in minute (Bromage-3)

Mean time taken for maximum motor blockade	Group-D	Group-F	P value FvsD
Mean±SD	10.4±0.81	10.13±0.73	0.187
Minimum	10	8	
Maximum	12	12	

The mean time taken for maximum motor blockade in Group-D was 10.4±0.81min and Group-F was 10.13±0.73 min. Statistically there was no difference when Group-F was compared with Group-D (P value0.187)

Table 9: Mean duration of motor blockade in minutes

Mean duration of motor blockade in minutes	Group-D	Group-F	P value FvsD
Mean±SD	367.83±35.5	188±9.53	0.000
Minimum	300	170	
Maximum	420	205	

The mean duration of motor blockade in Group-D was 367.83±35.5min and Group-F was 188±9.53min. Statistically there was highly significant difference when Group-F was compared with Group-D (P<0.000)

Statistically there was no significant difference in HR measured at various intervals throughout the surgery among the groups (P>0.05). Statistically there was no significant difference in SBP (mm of Hg) measured atvarious intervals throughout the surgery among the groups (P>0.05).

. Statistically there was no significant difference in DBP (mm of Hg) measured at various intervals throughout the surgery among the groups (P>0.05).. Statistically there was no significant difference in MAP (mm of Hg) measured at various intervals throughout the surgery among the groups (P>0.05).

In present study there was no statistically significant difference in the adverse effects throughout the procedure when Group-D was compared with Group-F. 4 patients in Dexmedetomidine group, 2 patients in Fentanyl group developed bradycardia which was managed by Inj. Atropine 0.6 mg IV. 11 patients in Dexmedetomidine group, 7 patients in Fentanyl group developed hypotension which was managed by Inj. Mephenteramine 6mg IV incremental doses. 1 patient in Group-F developed vomiting which was managed by Inj. Ondonsetron 4mg IV.

IV. Discussion

The present study was conducted comparing the adjuvants Dexmedetomidine 5µg and Fentanyl 25µg along with 0.5% hyperbaric Bupivacaine 12.5mg intrathecally for elective lower abdominal and lower limb surgeries.

The common anesthetic technique used in this institution for lower abdominal and lower limb surgeries is spinal anesthesia. Hyperbaric Bupivacaine 0.5% is used in India for spinal anesthesia for its duration of action and minimal incidence of transient neurological symptoms. In this institution, 12.5mg of hyperbaric Bupivacaine is the dose that is regularly used for lower abdominal and lower limb surgeries. Bupivacaine alone will produce a duration of sensory block up to 90-100 minutes. Hence, Bupivacainealone may not be sufficient to provide postoperative analgesia for these patients. Adjuvants are added along with Bupivacaine for prolonging the postoperative analgesia.Opioids are the most popular additives used for this purpose.

Other than Morphine, Fentanyl is the most commonly used opioid for prolonging the duration of intrathecal Bupivacaine. The addition of various doses of Fentanyl intrathecally as an adjuvant to spinal anesthesia produces faster onset time, decreases the somatic pain, visceral pain, improved intra-operative analgesia, and excellent qualityof perioperative analgesia . Fentanyl 25µg as an adjuvant to Bupivacaine is the usual dose administered by various authors· But the drawback of Fentanyl is its short duration of postoperative analgesia, side effects like pruritis, respiratory depression, increased incidence of postoperative nausea and vomiting. Because of these drawbacks of Fentanyl, there is a requirement for a suitable adjuvant that could produce a prolonged duration of postoperative analgesia with minimal side effects.

α2 agonists like Clonidine and Dexmedetomidine have been used as additives along with 0.5%

hyperbaric Bupivacaine for spinal anesthesia. Dexmedetomidine has been used as an intrathecal adjuvant for spinal anesthesia in various doses from 3 to 15µg. . Dexmedetomidine has been approved by the US food and drug administration as an intravenous sedative for mechanically ventilated adult intensive care unit patients. Its intrathecal use is off label. Various clinical studies using Dexmedetomidine as an adjuvant by intrathecal route with Bupivacaine have been found it to be safe without producing any neurological deficit on short-term followup. Dexmedetomidine is more specific to α_2 adrenergic receptor. Dexmedetomidine at a dose of 5µg has been used in more number of studies. Its use in human studies has also shown promising results in terms of early sensory and motor blocks and enhanced postoperative analgesic effects. Not many studies have been done comparing the usefulness of Dexmedetomidine with commonly used Fentanyl. Hence, in present study, the effectiveness of Dexmedetomidine 5µg with Fentanyl 25µg as additives to 0.5% hyperbaric Bupivacaine for intrathecal use in patients undergoing lower abdominal and lower limb surgeries were compared.

Demographic data: In the present study, there was no significant difference among the two groups, i.e., Dexmedetomidine group and Fentanyl group, regarding the patients' age, height, and weight. This study also did not find any statistically significant difference regarding the mean duration of surgery.

The onset of sensory blockade

The present study showed that the mean time taken for the onset of the sensory block was 1.73±0.450min in Group-D and 1.07±0.254min in Group-F. Statistically, there was a highly significant shorter onset time of sensory blockade in Group-F compared to Group-D (P<0.000).

This study compares with the study conducted by **Al-Mustafa M et al.**[3],**Abdelhamid S A et al**. [7], **Halder S et al**. [9], who also found a statistically significant difference in the mean onset of the sensory block between the Dexmedetomidine group and bupivacaine group.

Time taken for the maximum sensory blockade

roup- D and Our study's mean time for the maximum sensory blockade was 9.86±0.89min in G10.13±0.73min in Group-F. Statistically, there was no noticeable difference among the groups.

The present study compares with the studies conducted by **Gupta R et al**. [1] **Al Ghanem S M et al.**[2] and **Mahendru V et al**. [6], who also found no statistically significant difference in the mean time taken maximum sensory blockade between Dexmedetomidine group and Fentanyl group.

In the study conducted by **Gupta R et al**. [1], the time taken for the maximum sensory block was higher than in the present study between the Dexmedetomidine group andFentanyl group. This was probably because of spinal anesthesia given in sittingposition, and time taken to bring the patients to the supine position was not mentioned.The time of checking for the maximum sensory block was not mentioned after bringingthe patients back to a supine position. Hence probably the difference.

The maximum level of sensory blockade achieved

In the present study, 27 patients in Group-D and 25 patients in Group-F have attained a T4 level of block. Statistically, there was no significant difference when Group-D was compared with Group-F. The present study compares with the studies conducted by **Gupta R et al.** [1] and **Al-Ghanem S M et al.** [2] wherein they have also not found a statistically significant difference between Dexmedetomidine and Fentanyl group.

Mean time taken for sensory regression by two segments

The mean time taken for regression of sensory block by two segments in Group-D was 137.93±11.5min, and in Group-F was102.66±8.66min. Statistically, there was a noticeable increase in time taken for sensory regression by two Group-D segments compared to Group-F.

The present study compares with the studies conducted by, **Gupta R et al. [1], Tarbeeh G A et al**.[5], and **Khan A L et al**. [10] who also found a significant difference in the mean time taken for two segments sensory regression between the Fentanyl group and Dexmedetomidine group.

In the study done by **Kanazi et al.** [4], the mean time taken for sensory regression bytwo segments in the Bupivacaine group was 80±28 minutes, and in Dexmedetomidine group was 122±37min, which compares with the present study.

The mean time taken for a sensory block to regress to S1

The time taken for a sensory block to regress to S1 in our study was 396.80±30.87min in Group-D and 226.50±13.62min inGroup-F.There was a significant increase in meantime taken for regression of sensory block to S1 in Group-D compared to Group-F.

The present study compares with the study conducted by **Tarbeeh G A et al**. [5], who have also found a statistically significant difference in the Fentanyl group (198±52min) and Dexmedetomidine group (300±82min) when compared to the Bupivacainegroup(165±34min).

Mean duration of analgesia

In our study, the mean duration of analgesia in Group-D was 303.33±35.38min and Group-F was 201.16±8.49min. In the present study, the mean duration of analgesia in Group-D was higher and statistically significant compared with the Fentanyl group. Our study correlates with the study conducted by **Gupta R et al**. [1] (Dexmedetomidine group 251±30min and Fentanyl group 168±15min), **Tarbeeh GA et al[5].** (Dexmedetomidine group 450±84min and Fentanyl group 280±61min). **Khan A L et al**. [10] (Dexmedetomidine group 280±7.8min and Fentanyl group 173.8±8min), and

Mean time taken for onset of motor blockade

This study's mean time taken for the motor blockade's onset in Group-D was 1.10±0.30min, and Group-F was 1.03±0.18min. There was no significant difference among the groups regarding the mean time taken for the motor blockade onset. Hence the onset time of motor blockade was prolonged in their studies compared to the present study.

Mean time taken for maximum motor blockade

This study's mean time taken for the maximum motor blockade in Group-D was 10.4±0.81min, and Group-F was 10.13±0.73min. Statistically, there was no significant difference among the groups regarding the mean time taken for the maximum motor blockade. In a study conducted by **Mahendru V et al**. [6], the mean time taken for the motor blockade in the Fentanyl group was 9±3min, and the Dexmedetomidine group was 9.7±3.2min. Statistically, there was no significant difference in the mean time taken for onset of motor block and hence compares with our study. In a study conducted by **Gupta R et al**. [1], the mean time taken for the maximum motor blockade was 11.6±1.8min in Group-D, 11.2±1.3min in Group-F, and also did not find a statistically significant difference that correlates with our study.

Mean duration of motor blockade

In the present study mean duration of the motor blockade in Group-D was 367.83±35.5min and Group-F was 188±9.53min. Statistically, there was a significant increase in the motor blockade's mean duration in Group-D compared to Group-F. Our study's mean duration of motor blockade was prolonged in Group-D and statistically significant compared with Group-F. Our study compares with studies conducted by, **Gupta R et al.** [1], Al-**Ghanem S Met al** [2] and **Tarbeeh G A et al**. [5] **Mahendru V et al.** [6]. They also had found a statistically significant difference when the Dexmedetomidine group was compared with the Fentanyl group.

Hemodynamic parameters

In the present study, there was a statistically insignificant difference in the hemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure throughout the surgery when Group-D compared with Group-F. In present study, 2 patients in Group-F, 4 patients in Group-D developed significant bradycardia, which was statistically not significant. In our study, seven patients in Group-F and 11 patients in Group-D developed significant hypotension, which was statistically insignificant. The present study compares with the studies conducted by and **Gupta R et al.** [1] **Al Ghanem S M et al.** [2], **Kanazi et al.** [4], , **Tarbeeh G A[5] Mahendru V et al.** [6], **Makwana J [8]** and also did not find a significant difference statistically.

Adverse effects

In the present study, there was a statistically insignificant difference in the adverse effects throughout the procedure when Group-D was compared with Group-F. Thepresent study compares with the study conducted by **Gupta R et al.** [1], **Al Ghanem S M et al**. [2], **Kanazi et al**. [4], **Tarbeeh G A[5] and Mahendru V et al.** [6] who also did not find a statistically significant difference. In our study, one patient in Group-F had vomiting, which was statistically not significant.

V. Conclusion

From the present study, it can be concluded that both Fentanyl and Dexmedetomidine will lessen the time of

onset of sensory block and motor block, prolong the time for regression by two segments, the duration of sensory block, and motor block, andduration of analgesia compared to Bupivacaine alone.
However, Dexmedetomidine as an adjuvant produces more duration of sensory block, motor block, and duration of analgesia compared to Fentanyl as an additive.
Both Fentanyl and Dexmedetomidine as adjuvants do not produce significant hemodynamic changes, with minimal effects on ventilation and oxygenation. They produce a lesser incidence of pruritus and postoperative nausea and vomiting.
Hence it is concluded that Dexmedetomidine is better than Fentanyl as an adjuvant to 0.5% hyperbaric Bupivacaine for spinal anesthesia.

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