



Original Research Article

Comparison of dexmedetomidine and fentanyl as adjuvants to 0.5% hyperbaric bupivacaine in spinal anesthesia in elective lower abdominal surgeries

V Sai Divya¹, Rajola Raghu¹, P Indira^{1,*}, Sadhana Roy¹¹Dept. of Anaesthesiology, Osmania Medical College and Hospital, Hyderabad, Telangana, India

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ABSTRACT

Spinal anesthesia has become most commonly used and choice of anaesthesia for surgeries on lower half of body after first planned spinal anaesthesia for surgery in man was administered by August Bier (1861–1949) on 16 August 1898, in Kiel(1), Germany. Coadministration of adjuvant drugs improve the quality and duration of anesthesia and analgesia and patient safety.

Aim of Study: To compare effects of Dexmedetomidine and Fentanyl as adjuvants to 3ml of 0.5% heavy bupivacaine injected intrathecally, in lower abdominal surgeries.

Design of the Study: Prospective randomized comparative study.

Materials and Methods: The study was approved by ethics committee and was conducted in 100 randomly selected patients posted for elective lower abdominal surgeries in the age group 18-60yrs belonging to both sex. Patients were divided into two groups- Group D (n=50) - received 5µg Dexmedetomidine+3ml 0.5% heavy bupivacaine, Group F(n=50)-received 25µg Fentanyl +3ml 0.5% heavy bupivacaine, intrathecally respectively.

Observations and Results: In group D patients onset of sensory block was significantly faster 2.62 ± 0.56 mins ($p < 0.001$) with better haemodynamic stability, intraoperative sedation, less incidence of side effects and analgesic sparing effect in post operative period when compared to group F.

Conclusion: α_2 adrenergic agonist dexmedetomidine is a valuable adjunct to spinal anaesthesia it augments quality of spinal anaesthesia provides intraoperative sedation and hemodynamic stability.

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1. Introduction

Anaesthesiology is practice of medicine dedicated to pain relief and total care of surgical patient perioperatively. Pain is defined as "an unpleasant sensory and emotional experience associated with, actual or potential tissue damage."¹ Anaesthesiologists challenge is to devise a technique for postoperative analgesia with least side effects. August Bier (1861-1949), a German surgeon, is "Father of Intrathecal Anesthesia" popularized spinal anesthesia² and it is choice of anaesthesia in lower abdominal surgeries. Advantages are rapid onset of anaesthesia, optimal operating conditions, effectively attenuates neuroendocrine stress response, control of immediate post-operative pain

and cost effective. Local anesthetics are limited by short duration of action and there is early demand for rescue analgesics. Adjuvants³ are added to improve quality and duration, provide better postoperative analgesia and patient comfort.⁴ Local anesthetic adjuvants (46) include classical opioids to a wide range group of drugs with varying mechanisms of action. Adjuvants decrease dose of local anaesthetic and their side effects. (myocardial depression, hypotension, bradycardia, heart block, and ventricular arrhythmias). A common problem during lower abdominal surgeries under spinal anesthesia is visceral pain, nausea, and vomiting.⁵ Fentanyl is μ receptor agonist 80 times more potent than morphine as an analgesic^{6,7} added to spinal 0.5% heavy bupivacaine improves quality of spinal analgesia, reduces visceral and somatic pain.⁷ However

* Corresponding author.

E-mail address: dudyalaindira@yahoo.com (P. Indira).

their addition may have side effects like pruritus, respiratory depression, urinary retention, postoperative nausea and vomiting which limits their use.⁸ Dexmedetomidine is highly selective α_2 -agonist, S-enantiomer of veterinary sedative medetomidine.^{9,10} Food and Drug Administration has approved its use for short-term ICU sedation, it is reported to provide sedation that parallels natural sleep, anxiolysis, analgesia, sympatholysis, and anaesthetic-sparing effect with minimal respiratory depression. α_2 -agonists produce clinical effects by binding to G-Protein-coupled α_2 -AR.¹¹ It was under evaluation as neuraxial adjuvant as it provides prolonged analgesia, hemodynamic stability with minimal side effects. Based on earlier human studies, it was hypothesized, dexmedetomidine 5 μ g added to 0.5% heavy bupivacaine produces profound postoperative analgesia with minimal side effects.^{12–14} In this study we compared 5 μ g dexmedetomidine with fentanyl 25 μ g added to 3ml 0.5% hyperbaric bupivacaine as adjuvants in spinal anaesthesia.

2. Materials and Methods

A randomized comparative double blind study was carried out at Osmania General Hospital during 2016-2018. Institutional Ethics Committee has approved the study which included 100 ASA I, II patients scheduled for elective lower abdominal surgeries (Appendectomy, inguinal herniorraphy, ovarian cystectomy, TAH, vaginal hysterectomy, cystolithotomy, cystolithotripsy, ovarian cystectomy, internal urethrotomy etc.) under spinal anaesthesia.

2.1. Inclusion criteria

1. ASA physical status class I and II.
2. Age between 18 – 60 years of either sex.

2.2. Exclusion criteria

1. ASA grade III and IV
2. Infection at the site of injection
3. Coagulopathy or anticoagulation
4. Congenital anomalies of lower spine
5. Active disease of CNS
6. History of allergy to local anesthetics

Patients were allocated into two groups by simple randomization technique, based on study drugs assigned to each group.

Group D (50 no's) - 5 μ g Dexmedetomidine (5 μ g added by taking 50 μ g in a insulin syringe) + 3ml 0.5% heavy bupivacaine hcl.

Group F (50 no's) - 25 μ g Fentanyl+ 3ml 0.5% heavy bupivacaine hcl.

At preanaesthetic assessment, all patients were evaluated and investigated for systemic diseases. Participants were

explained about SAB procedure and educated about using 'VAS'. A written and informed consent was obtained from all participants in the study. Pre-op preparation of patients included overnight NPO, premedication -Tab. Rantidine 150 mg, Tab. Alprazolam 0.5 mg.

2.3. Procedure

On day of surgery, anaesthesia work station and emergency cart were kept ready in OR. On arrival of patient on OR table, 18G iv access was secured on left forearm, patient was connected to multi parameter monitor and baseline vitals were recorded, preloading was done with 15ml/kg Ringer's Lactate 15 mins prior to start of procedure. Subarachnoid block was performed under aseptic precautions with patient in right lateral position using 26G Quincke's spinal needle, test drugs assigned to study groups were deposited intrathecally and patient turned supine immediately. Time of onset of T10 sensory block and peak sensory block was noted using pin prick method, Motor block was assessed with Modified Bromage scale and time of onset of bromage 3 motor block was noted. NIBP, ECG NIBP, ECG, HR and SpO₂ was recorded every 2 minutes for first 10 minutes, every 10 minutes for next 50 min and every 15 minutes till end of surgery.

Bromage Scale:

Bromage 0 - patient is able to move the hip, knee and ankle.

Bromage 1 - patient is unable to move the hip but is able to move the knee and ankle.

Bromage 2 - patient is unable to move the hip and knee but able to move the ankle.

Bromage 3 -patient is unable to move the hip, knee and ankle.

Modified Ramsay Sedation Score for assessing 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.

Intraoperatively all the patients were observed for

1. Hypotension described as > 20% fall of baseline blood pressure, treated with 200 ml Ringer's Lactate bolus and 6mg ephedrine i.v.,
2. Bradycardia defined as HR < 50 bpm, treated with 0.5 mg atropine iv.
3. Respiratory depression defined as respiratory rate < 9 breaths/min and SpO₂ < 90% on room air, incidence was recorded in data sheet for analysis.

4. Side effects.

Regression time of sensory block and motor blockade to reach modified Bromage 0 was noted.

Visual analogue scale used for assessing postoperative pain. VAS > 6 rescue analgesic was given and time noted.

2.4. Statistical methods

Statistical analysis was done by Statistical package for social sciences (SPSS) version 17.0, (SPSS Inc, Chicago, IL) statistical analysis software.

Results on continuous measurements are presented on Mean $\pm$ SD (Min-Max) and categorical measurements are presented in Number (%). Significance is assessed at 5% level. Student t test (two tailed, independent) was used to find significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. (43,44) p value was determined.

P > 0.05 is not significant.

P < 0.05 is significant.

P < 0.001 is highly significant

3. Observations and Results

The variables of subarachnoid block were compared in both groups it was found the time to attain T₁₀ level significantly lower in group D (02.62 $\pm$ 0.56 min, p < 0.001). The difference in highest level of sensory block (T4 and T5), time to reach highest level, time to onset of bromage 3 was insignificant. Time to regression to bromage was significantly delayed in Group D (419.70 $\pm$ 16.85min, p < 0.001).

Hemodynamic stability in both study groups was comparable throughout study period, incidence of hypotension and bradycardia was seen in 14 patients and 7 patients respectively in group D, there were no other side effects noted.

Sedation score in the perioperative period was significantly more at 60min (3.00 $\pm$ 0.00, p value < 0.001) and 90 mins (3.40 $\pm$ 0.49, p value < 0.001).

Postoperative pain score was significantly lower ('p' < 0.001) in dexmedetomidine group and need for rescue first 24hrs was less.

4. Discussion

Post operative pain and suffering results in significant physiological, psychological, economic and social adverse effects.¹⁵ Spinal anaesthesia is a popular technique for lower abdominal surgeries and is effective in immediate post-operative pain relief. Various analgesic regimens have been used to ensure adequate postoperative pain relief as local anaesthetics have short duration of action and potential to produce deleterious effects like cardiac arrhythmias, central nervous system depression,

seizures and allergic reactions.^{16–18} Co-administration of adjuvants prolong duration of sensory-motor block, limit cumulative dose requirement of local anaesthetics improve efficacy and contribute in their own special manner to potentiate analgesic effect of local anaesthetics.¹⁹ Neuraxial administration of opioids as adjuvants is one method for postoperative pain management, which allows early ambulation, and decrease length of hospital stay however they are often associated with side-effects like nausea, vomiting, respiratory depression and hyperalgesia. Intrathecal Fentanyl as adjuvant to bupivacaine is an established method,^{20,21} it has rapid onset,^{22,23} enhances intra and postoperative analgesia without prolonging motor block.²² Fentanyl is more lipid soluble and rapidly eliminated from CSF making late respiratory depression less likely. The clinical experience gained in use of α 2-adrenoreceptor agonists intrathecally is described with clonidine, clinical studies are needed to prove efficacy, safety, suitable dose of dexmedetomidine as an adjuvant spinal local anaesthetics. α 2-agonists bind to presynaptic C-fibers, postsynaptic dorsal horn neurons, complementary action of local anaesthetics and α 2 agonists at spinal level accounts for profound analgesic properties. Intrathecal α -2 receptor agonists have been found to significantly prolongs duration of spinal anaesthesia, have antinociceptive action for both somatic and visceral pain.²⁴ Fentanyl and Dexmedetomidine were compared as adjuvant to heavy bupivacaine in our study, Group F received 3ml of 0.5% heavy bupivacaine and 25 μ g Fentanyl, Group D received 3ml of 0.5% heavy bupivacaine and 5 μ g Dexmedetomidine intrathecally in patients posted for elective infra umbilical surgeries.

4.1. The following parameters were observed during study

1. Time of onset of action.
2. Highest level of sensory and motor blockade.
3. Time of onset of Bromage 0.
4. Intraoperative heart rate, Blood pressure, SpO2.
5. Intraoperative sedation.
6. Regression to Bromage 3.
7. Postoperative requirement of analgesia.

Study results demonstrate 25 μ g Fentanyl prolongs duration of bupivacaine induced sensory block, as reported in study by Wang et al.,²⁵ in parturients undergoing caesarean delivery intrathecal Fentanyl didn't enhance onset of Bupivacaine induced spinal block as reported by Hunt et al.,²⁶ Opioids and local anaesthetics exert their antinociceptive effect in spinal cord by different mechanisms. Fentanyl, exerts its action by opening K⁺ channels and reducing Ca²⁺ influx, result in inhibition of transmitter release. It also has a direct postsynaptic effect, causing hyperpolarisation and a reduction in

Table 1: Age, gender, height and weight distribution of patients in the study

Age distribution			Gender distribution				
	Group F		Group D		Group F	Group D	
	No	%	No	%	M(%) / F(%)	M(%) / F(%)	
18-20yrs	02	4	0	0	25 (50%) / 25(50%)	25(50%)/ 25(50%)	
21-30yrs	03	6	04	8			
31-40yrs	13	26	26	52			
41-50yrs	22	44	14	28			
51-60yrs	08	16	05	10			
>60yrs	02	4	01	2			
Total	50	100	50	100			
Mean±SD	43.76±10.33		40.86±9.27				

Study participants in both groups were comparable in demographic profile

Table 2: Comparison of variables in subarachnoid block

Variables	Group F	Group D	'p' value
Time from injection to T10(min)	03.38±0.83	02.62±0.56	<0.001
Time from injection to highest Sensory (min)	11.47±1.23	11.72±1.23	0.314
Onset of Bromage 3 (min)	10.38±1.08	10.59±1.00	0.317
Regression to bromage 0 (min)	152.90±8.31	419.70±16.85	<0.001

Table 3: Comparison of systolic blood pressure (mmHg) between two groups

SBP(mmHg)	Group F	Group D	'p' value
Pre op	128.60±11.70	126.20±9.54	0.264
2min	125.12±12.11	119.40±10.65	0.014
4min	119.10±11.34	114.84±10.85	0.058
6min	115.24±9.77	112.76±10.84	0.233
8min	112.42±9.04	110.92±10.86	0.455
10min	110.22±9.87	110.50±10.50	0.891
20min	109.46±9.70	109.38±10.77	0.969
30min	107.66±9.49	108.34±10.57	0.736
40min	106.64±9.98	107.32±10.20	0.737
50min	106.82±10.18	107.12±9.75	0.881
60min	108.98±9.74	107.82±9.20	0.542
75min	111.24±9.57	108.60±8.88	0.156
90min	114.58±8.32	110.56±8.55	0.019

Table 4: Comparison of diastolic blood pressure (mm Hg) between two groups

DBP (mmHg)	Group F	Group D	'p' value
Pre op	80.10±8.58	80.78±7.81	0.679
2minutes	77.38±9.68	74.18±9.22	0.094
4minutes	72.46±8.56	71.06±9.48	0.440
6minutes	69.04±8.65	69.44±9.56	0.827
8minutes	65.76±7.87	67.74±10.31	0.283
10minutes	62.30±8.39	66.68±10.31	0.022
20minutes	60.92±9.23	65.12±9.96	0.031
30minutes	61.36±7.40	64.80±9.66	0.048
40minutes	60.90±8.25	64.94±9.62	0.026
50minutes	61.28±8.50	64.76±9.28	0.053
60minutes	62.98±8.79	65.16±8.90	0.221
75minutes	65.75±7.53	65.62±8.30	0.933
90minutes	69.00±7.54	67.18±8.42	0.258

Table 5: Comparison of MAP (mmHg) between two groups

MAP (mmHg)	Group F	Group D	'p' value
Pre op	97.02±9.99	94.98±7.02	0.238
2minutes	93.29±10.02	89.25±8.97	0.036
4minutes	88.00±8.86	85.65±9.27	0.198
6minutes	84.44±8.48	83.88±9.50	0.757
8minutes	81.31±7.67	82.13±10.08	0.648
10minutes	78.27±8.37	81.28±9.98	0.105
20minutes	77.10±8.63	79.87±9.84	0.138
30minutes	76.79±7.38	79.31±9.50	0.142
40minutes	76.14±8.15	79.06±9.35	0.099
50minutes	76.46±8.49	78.88±8.95	0.169
60minutes	78.31±8.62	79.38±8.41	0.533
75minutes	80.91±7.65	79.94±7.98	0.541
90minutes	84.19±7.14	81.64±8.02	0.096

Table 6: Comparison of Heart Rate in study groups

HR(bpm)	Group F	Group D	'p' value
Pre op	82.68±12.42	84.36±13.71	0.522
2minutes	82.04±12.16	83.36±13.94	0.615
4minutes	81.02±11.16	83.82±14.32	0.278
6minutes	79.78±10.72	83.02±14.03	0.198
8minutes	78.58±9.67	80.34±12.51	0.433
10minutes	77.60±8.79	77.75±10.80	0.938
20minutes	76.42±8.14	76.26±11.38	0.936
30minutes	75.46±7.70	75.48±11.20	0.992
40minutes	74.68±7.67	74.92±10.87	0.899
50minutes	74.48±7.70	74.92±9.70	0.802
60minutes	74.18±7.57	74.98±8.64	0.624
75minutes	73.40±7.57	74.90±8.54	0.355
90minutes	72.78±7.11	73.84±8.22	0.492

Table 7: Comparison of RR and SpO₂ between two groups

Variables	Group F	Group D	'p' value
Respiratory rate (RR)	16.10±1.61	16.10±1.61	1.000
SpO ₂	97.92±0.75	97.92±0.75	1.000

Table 8: Side-effects noted in study groups

Side-effects	Group F (n-50)		Group D (n-50)	
	No.	%	No.	%
Nausea	3	6	0	0.0
Vomiting	1	2	0	0.0
Pruritis	3	6	0	0
Hypotension	8	16	14	28
Bradycardia	0	0.0	7	14
Urinary retention	0	0.0	0	0.0
Respiratory depression	0	0.0	0	0.0

Table 9: Comparison of modified Ramsay sedation score

MRSS	Group F	Group D	'p' value
30mins	2.00±0.00	2.00±0.00	1.000
60mins	2.00±0.00	3.00±0.00	<0.001
90mins	2.16±0.37	3.40±0.49	<0.001
120mins	2.14±0.35	2.00±0.00	0.006
150mins	2.00±0.00	2.00±0.00	1.000
180mins	2.00±0.00	2.00±0.00	1.000

Table 10: Comparison of visual analogue scale

VAS	Group F	Group D	'p' value
6hours	3.50±0.51	0.00±0.00	<0.001
12hours	5.90±0.97	3.50±0.51	<0.001
18hours	7.28±0.95	5.52±0.51	<0.001
24hours	7.24±0.96	3.62±0.69	<0.001

neuronal activity. Bupivacaine, acts mainly by blockade of voltage gated Na⁺ channels in axonal membrane, interfere with synaptic transmission by a presynaptic inhibition of Ca⁺⁺ channels in addition to their effects on nerve conduction. A combination of these effects may explain observed synergism between Bupivacaine and Fentanyl in our study group. Intrathecal fentanyl as adjuvant reduces visceral and somatic pain.²⁷ Talke et al.,²⁸ observed antishivering property of α -2 adrenergic agonists, shivering was not observed in both the study groups. Intrathecal Fentanyl as an adjuvant to bupivacaine prolonged sensory block without prolonging motor block though fewer patients in this group demanded pain relief,²⁹ Harbhejsingh et al., showed Fentanyl, 25 μ (0.3 μ /kg) intrathecally, reduced analgesic requirement without increasing incidence of side effects nausea or pruritus and desaturation in early postoperative period,²⁹ number of studies have shown 25 μ Fentanyl provides maximum duration of post-operative analgesia with minimal side effects like respiratory depression and pruritus, in present study pruritus was observed in few patients which is insignificant. Varrassi et al, noted 25 μ g Fentanyl in spinal anaesthesia, in non premedicated elderly males did not alter respiratory rate, ET_{CO2}, minute ventilation, respiratory drive or ventilatory response to CO₂, concluded 50 μ g Fentanyl causes an early respiratory depression.³⁰ Hala EA Eid et al., 15 μ g dexmedetomidine intrathecally showed significantly higher sedation scores which can be beneficial for patients undergoing lengthy complex surgeries as an alternative to epidural or prolonged general anesthetics.³¹ However, such high sedation scores may be harmful in elderly and high risk surgical patients owing to excessive sedation and respiratory depression.

Belzarena et al., Fentanyl 0.5 μ /kg and 0.75 μ /kg intrathecally, increased duration of postoperative analgesia in parturients following caesarean delivery (640 ± 141 min and 787±161 min, respectively); however, it was associated with a decrease in respiratory rate and increased incidence of sedation and pruritus.³² Fentanyl 50-100 μ g in epidural provides postoperative analgesia 3-4 hrs duration, similar to duration of analgesia following 25 μ g dose of subarachnoid Fentanyl.

Rajni Gupta, Reetu Verma, Jaishri Bogra et al., compared 5 μ g Dexmedetomidine with 25 μ g Fentanyl as adjuvants to spinal heavy bupivacaine, found dexmedetomidine is associated with prolonged motor and sensory block, hemodynamic stability, reduced demand for rescue

analgesics in 24hrs as compared to Fentanyl³³ which are similar to our study. Sedation score was more in group D patients (3.8 ± 0.5) as compared to group F (2.2±0.53) which is statistically significant (P<0.05). The findings correlate with our study mean sedation score in group D (3.40 ± 0.49) was significant (p<0.001) compared with group F (2.16 ± 0.37), postoperative analgesic requirements in first 24hrs was significantly less in Group D (p <.001). Incidence of nausea vomiting and pruritis was known in our study but was insignificant. α -2adrenergic agonist also have antishivering property as observed by Talke et al and Maroof M et al., there was no incidence of shivering in our study.^{34,35} Epidural dexmedetomidine 2 μ g/kg for postoperative analgesia in humans did not result in any neurologic deficits³⁶ Fukushima et al., Dexmedetomidine 3 μ g or 30 μ g clonidine added to 13 mg spinal bupivacaine produced same duration of sensory and motor block with minimal side effects in urologic surgeries Kanazi et al., from this study, we assumed 3-5 μ g dexmedetomidine and 30-45 μ g clonidine are equipotent as adjuvants to spinal Bupivacaine.³⁷ Both Fentanyl and Dexmedetomidine provided good quality intraoperative analgesia, clinically better in group D. Al-Ghanem et al., had compared 5 μ g Dexmedetomidine and 25 μ g Fentanyl as adjuvants 10mg isobaric Bupivacaine in vaginal hysterectomy and concluded that 5 μ g Dexmedetomidine produces more prolonged motor and sensory block. These findings correlate with our study, sensory and motor block duration was significantly longer in Dexmedetomidine group (419.70±16.85mins, p value <0.001) and good patient satisfaction.³⁸ Al-Mustafa et al., studied effect of Dexmedetomidine 5 μ g and 10 μ g with Bupivacaine in urological procedures, Dexmedetomidine prolongs duration of spinal anaesthesia in a dose dependent manner and attenuates visceral pain in abdominal surgeries under spinal anaesthesia. In our study also no patient perceived visceral pain in both D and F groups.³⁹

Rajni Gupta, Reetu Verma, Jaishri Bogra et al, (2011) used Dexmedetomidine 5 μ g as an intrathecal adjuvant to ropivacaine produces prolonged duration of motor and sensory block.⁴⁰ 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 observed in 14 patients of group D.⁴¹

5. Limitations of the study

1. Population involved includes young and otherwise healthy patients.
2. The effect in older patients with cardiovascular comorbidities are yet to be investigated.
3. This study also lacks an active control for systemic effects of Dexmedetomidine.

6. Recommendations

Further studies that compare effect of intrathecal and IV Dexmedetomidine on spinal Bupivacaine may also be warranted.

7. Conclusion

In conclusion, 5 µg dexmedetomidine is a good alternative to 25 µg fentanyl as an adjuvant to 0.5% heavy bupivacaine in spinal anesthesia. It provides a better quality of perioperative / intraoperative analgesia, hemodynamic stability, minimal side effects, and reduced demand for rescue analgesics in 24 hr as compared to Fentanyl. Hence, Dexmedetomidine seems to be a better choice as Intrathecal adjuvant with Bupivacaine.

8. Source of Funding

None.

9. Conflict of Interest

The authors declare that there is no conflict of interest.

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Author biography

V Sai Divya, Post Graduate

Rajola Raghu, Associate Professor

P Indira, Associate Professor

Sadhana Roy, Professor

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