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Original Research Article

A COMPARATIVE STUDY OF INTRATHECAL DEXMEDETOMIDINE AND BUPRENORPHINE AS ADJUVANT TOBUPIVACAINE IN SPINAL ANAESTHESIA

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Abstract

The supplementation of local anaesthetics with adjuvants to improve the efficacy of subarachnoid block has been recognised since long. The most preferred drug has been opioids, but newer drugs like dexmedetomidine has also been introduced and investigated as an effective adjuvant.

MATERIALS AND METHODS: The present study included 60 patients aged between 18-60 years classified as American Society of Anaesthesiologists (ASA) Physical Status (PS) I/II scheduled for elective lower abdominal surgeries. The patients were randomly allotted into two groups namely Group BB and Group BD of 30 each. Patientsin Group BB received 75µg of buprenorphine with 0.5% bupivacaine 15 mg intrathecally. Patients in Group BD received 5µg of dexmedetomidine with 0.5% bupivacaine 15 mg intrathecally. The onset time to peak sensory level, motor block, sedation, Haemodynamic variables, duration of motor block, analgesia and any adverse effects were noted.

RESULT: There was no significant difference between groups regarding demographic characteristics and type of surgery. The motor, sensory blockade and time of rescue analgesia were significantly prolonged in Group BD compared to GroupBB. The sedation level was higher in Group BD compared to GroupBB. There was no significant difference in haemodynamic variables although GroupBB had lower Heart Rate (HR) than Group BD.

CONCLUSION: Intrathecal dexmedetomidine when compared to intrathecal buprenorphine causes prolonged anaesthesia, analgesia with better degree of sedation and reduced need of rescue analgesics.

KEYWORDS: Buprenorphine; Lower abdominal surgery; α–2 adrenergic agonist

Introduction

The International Association for the study of pain(IASP) defined pain as "an unpleasant sensory or emotional experience associated with actual or potential tissue damage or described in terms of such damage"[1].

Spinal anaesthesia was first performed by August Bier on 16th August 1898 when he injected 3 ml of 0.5% Cocaine intrathecally. It is a simpletechnique which has many advantages

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over epidural anaesthesia. In addition, correct placement of the needle in the subarachnoid space is confirmed by a clearly defined end point (appearance of CSF).

Spinal anaesthesia with local anaesthetic agents is extensively used for lower abdominal surgeries. It provides the excellent pain relief as compared to intravenous or epidural route.

There are many advantages for spinal anaesthesia over general anaesthesia which makes it the anaesthesia of choice in current surgical practice. Many clinical studies support the fact that Postoperative morbidity and mortality may be reduced when neuraxial blockade is used either alone or in combination with general anaesthesia. Since it decreases the stay, it is cost effective for both patient and hospital. It is suitable for patients with respiratory diseases and helps in preventing intubation related problem like laryngospasm. It is also helpful in maintaining the airway patency and reduced blood loss.

Early return of gastro intestinal function following surgery can be considered as an added advantage. Other advantage may be reduced hypercoagulable state associated with surgery, increased tissue blood flow due to sympathectomy, decreased splinting which improves oxygenation, enhanced peristalsis, and reduced stress response to surgery due to suppression of neuroendocrine system [2].

Apart from the theoretical risk of infection to the brain, difficulty in finding the space in old age and bony abnormalities can pose a challenge to the anesthesiologist. The serious complication associated with spinal anaesthesia includes bradycardia, hypotension, prolonged motor block and high spinal [3]. It is related to the sympatholytic effect of local anaesthetic agents.

If the level of the block is higher, the sympatholytic effect will be more and leads to more serious complications. Though these effects cannot be abolished completely, they can be considerably minimized by using either low dose or low concentration of local anaesthetics. One of the main disadvantages is the limited duration of block achieved with local anaesthetics. To overcomethis, various adjuvants have been tried and used successfully.

This addition of adjuvant has further expanded the advantage of regional anaesthesia like

i) Rapid onset of action
ii) Reduces the local anaesthetic requirements
iii) Reduces the risk of local anaesthetic toxicity
iv) Prolongs the sensory block
v) Reduces the duration of motor block
vi) Improves the analgesic quality
vii) Improves the hemodynamic stability
viii) Inhibition of tourniquet pain
ix) Improved and prolonged duration of postoperative analgesia.

Opioids are the time honoured drugs which have been used for thispurpose. Morphine was the first opioid used intrathecally in 1979, followed by other opioids [4 5 6]. Buprenorphine is a centrally acting lipid soluble analogue of alkaloid thebaine. It exhibits analgesic property both at spinal and supraspinal levels [7]. It has been used for various surgeries at different doses for the pastfew decades. It has consistently proven to prolong the duration of anaesthesia[8,9

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,10] . At higher doses, it causes pruritus, drowsiness, nausea and vomiting [11].

MATERIALS AND METHODS

This study was conducted in Department of Anaesthesiology ,ESIC Medical College, Kalaburagi 60 ASA grade 1 or 2 patients undergoing elective lower abdominal surgeries like Hernia repair and appendicectomy under spinal anaesthesia. Before including the patients for the study, all patients were explained about the procedures anda written informed consent was obtained.

INCLUSION CRITERIA:

- Adult patients aged 18 - 60 years of either sex
- ASA 1 and 2 patients.
- Patients undergoing elective lower abdominal surgeries.

EXCLUSION CRITERIA:

- Patients with known contraindication for spinal anaesthesia.
- Patients with coagulation disorders or on anticoagulation therapy.
- Patients with cardiac disease, heart blocks and dysarrythmias
- Patients with betablockers & alpha antagonists.

PREOPERATIVE PREPARATION:

After routine preoperative assessment at the patients' waiting room in the OT, basal line readings of the vital parameters were recorded. Intravenous line started. The patients were randomly allocated into two groups of 30 each by using closed cover technique.

In the operating room, appropriate equipment for airway management and emergency drugs were kept ready. The horizontal position of the operatingtable was checked. Patients were shifted to the operating room and positioned Non-invasive blood pressure monitor, pulse oximeter and ECG leads were connected to the patient. Preoperative baseline systolic and diastolic blood pressure, mean arterial pressure, pulse rate, respiratory rate and oxygen saturation were recorded. Patients were preloaded with 10ml/kg of ringer lactate 15minutes prior to the subarachnoid block. On sitting position, the skin over the back was prepared with antiseptic solution and draped with sterile towel.

RESULTS

All 60 patients in two groups completed the study without any exclusion.
Inter group analysis was done and the results were as followed.

The collected data were analysed by chi square test and results obtained inthe form of range, mean and standard deviation. The probability value 'p' of less than 0.05 considered statistically significant.

Patient demographic data that includes age, sex, and duration of surgerybetween two groups were comparable.

Table 1: Age distribution

	Age in years			
	Group BB		**Group BD**	
Age group	**No.**	**%**	**No.**	**%**

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Below 30 years	6	20	8	26.7
31 – 40	9	30	6	20
41 – 50	6	20	9	30
Above 50	9	30	7	23.3
Total	30	100	30	100
Range	19 – 60 years		18 – 60 years	
Mean	42.33		40.57	
SD	12.88		13.22	
'p' value	0.875 Not significant			

The age distribution was in the range of 19-60 in Group BB and 18-60in Group BD. The 'p' value for mean age was not statistically significant (p value = 0.875).

AGE DISTRIBUTION

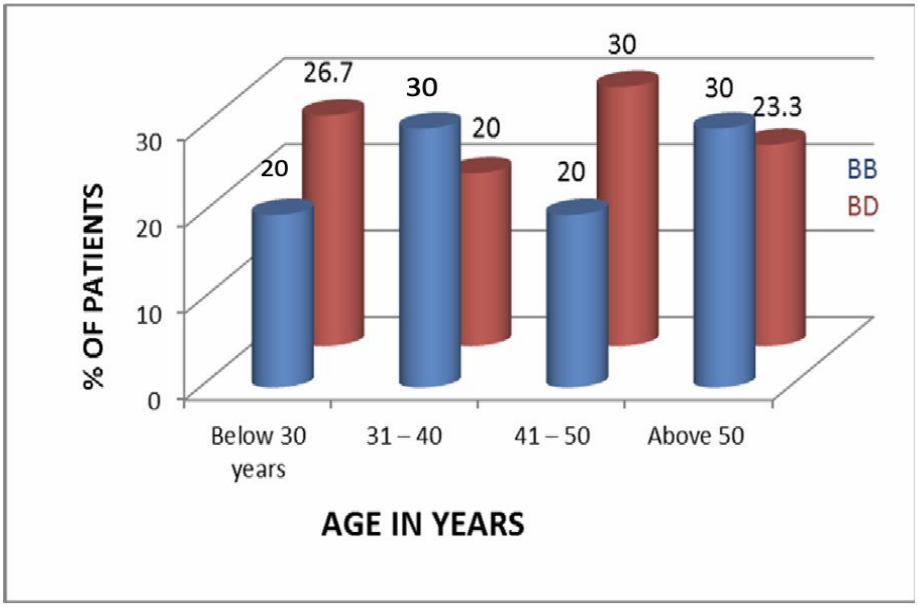

Table 2: Sex distribution

Sex	Group BB		Group BD	
	No	**%**	**No**	**%**
Male	25	83.3	23	76.7
Female	5	16.7	7	23.3
Total	30	100	30	100
'p'	0.752 Not significant			

Though male and female ratio is not equal in either group, statistics between the groups for sex distribution was not significant. The p value is 0.752.

EFFICACY OF THE TWO DRUGS

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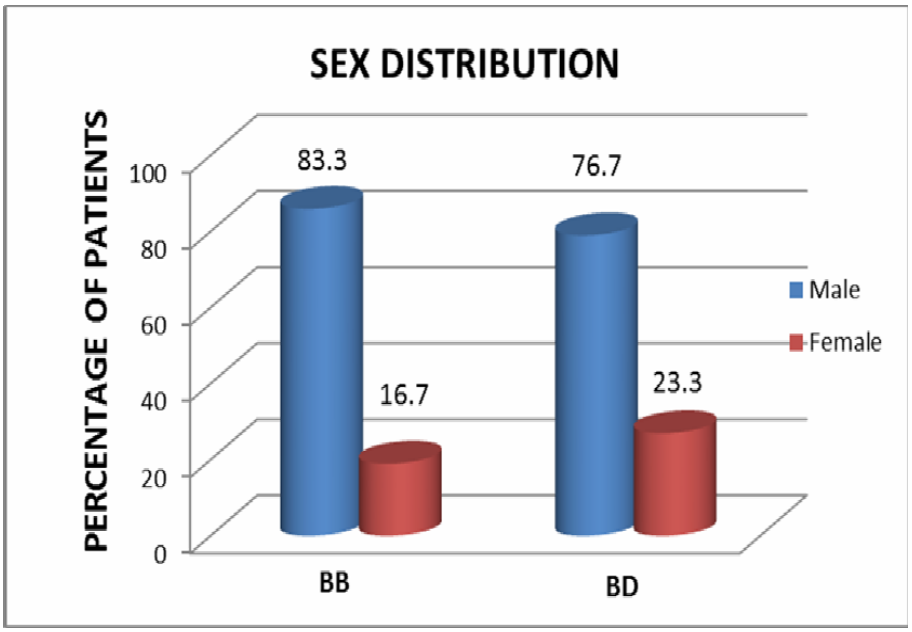

Table 3: Time of onset of sensory block

Parameter	Time of onset of sensory block(in minutes)	
	Group BB	**Group BD**
Range	3-4	2-3
Mean	3.47	2.57
SD	0.507	0.504
'p' value	0. 629 Not Significant	

The time of onset of sensory block was slower in Group BB (3.47± 0.507) when compared with Group BD (2.57± 0.504) and the p value was statistically not significant (0.629 > 0.05).

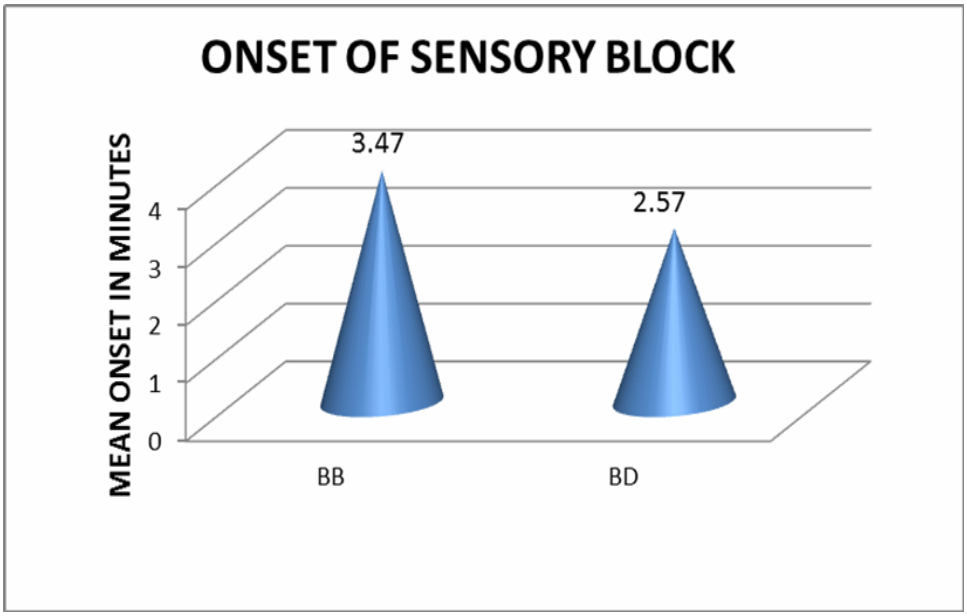

Table 4: Time of onset of motor block

	onset of motor block(in minutes)

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Parameter	Group BB	Group BD
Range	3-5	3-5
Mean	3.83	4.13
SD	0.817	0.78
'p' value	0. 775 Not Significant	

The average time taken for the onset of motor block was 3.83 minutes in Group BB and 4.13 minutes in Group BD. It was statistically not significant (p value 0.775 > 0.05).

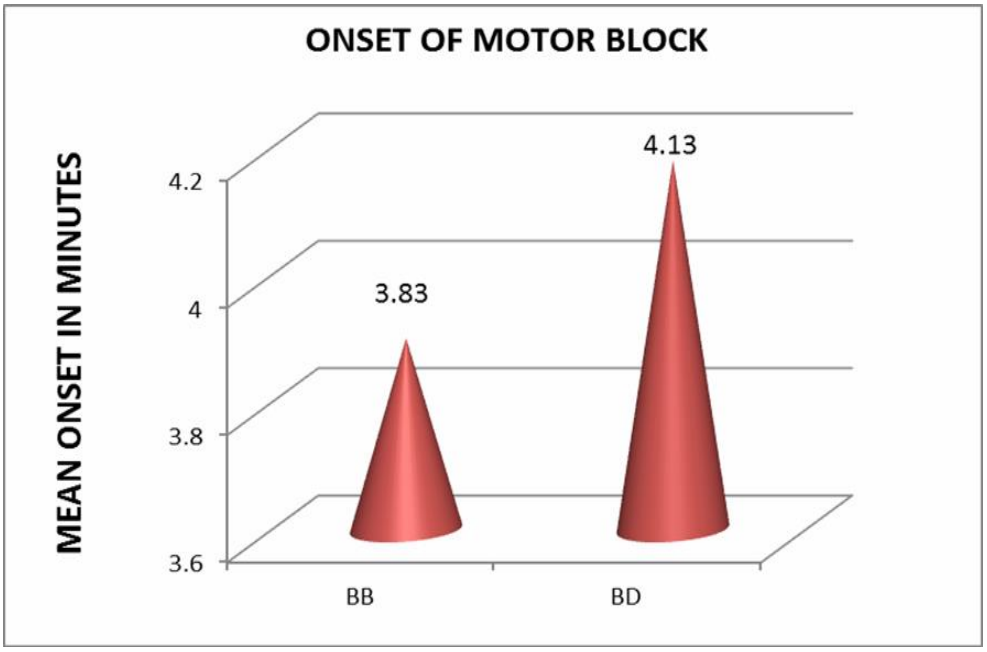

Table 5: Duration of Sensory block

Parameter	Duration of Sensory block(in minutes)	
	Group BB	Group BD
Range	303-360	480 – 520
Mean	332	502.13
SD	18.81	12.27
'p' value	0. 005 Significant	

The mean duration of sensory block was shorter in Group BB (332 ± 18.81) when compared with Group BD (502.13 ± 12.27). It was statistically significant (p value= 0.00 < 0.05). The mean duration of sensory block in Group **BD** is approximately ***51% longer*** than Group BB.

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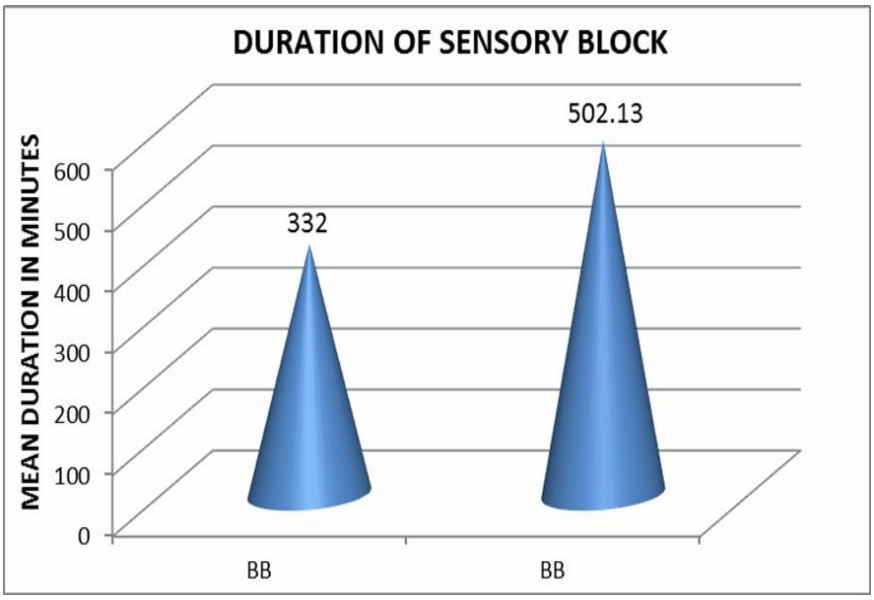

Table 6: Duration of motor block

Parameter	Duration of motor block(in minutes)	
	Group BB	**Group BD**
Range	293-360	413-460
Mean	298.63	432.33
SD	35.79	12.74
'p' value	0. 000 Significant	

The mean duration of motor block was shorter in Group BB (298.63 ± 35.79) when compared with Group BD (432.33 ± 12.74). It was statistically significant (p value = 0.00 < 0.05). The mean duration of motor block in Group **BD** is about approximately ***44% longer*** than Group BB.

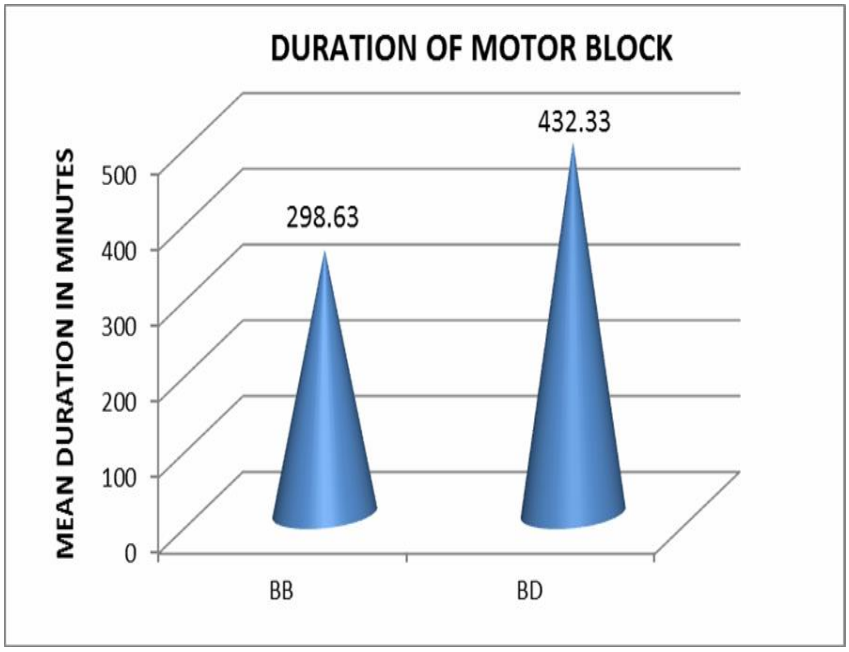

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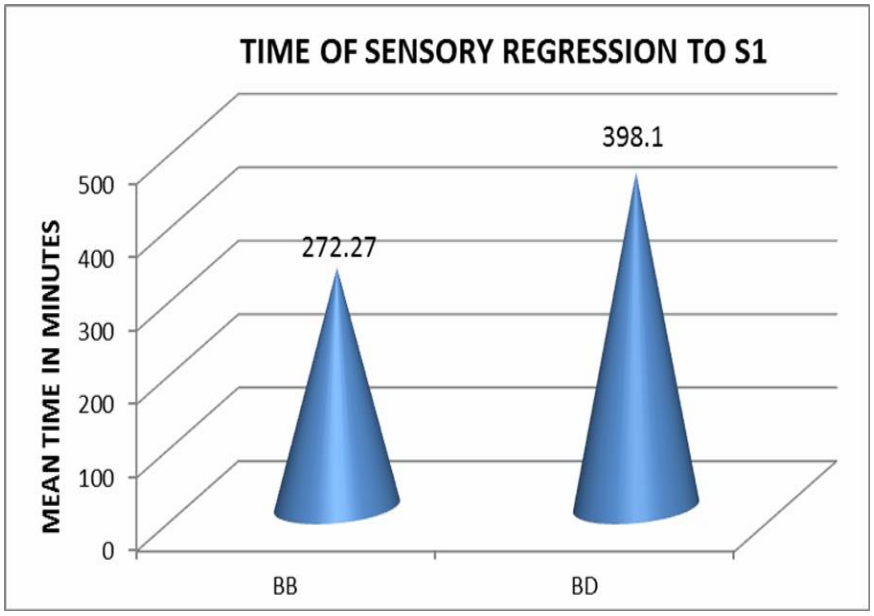
Table 7: Time of sensory regression to S1

Parameter	Time of sensory regression to S1(in minutes)	
	Group BB	**Group BD**
Range	250-299	389-409
Mean	272.27	398.1
SD	15.39	6.50
'p' value	0. 001 Significant	

The time of sensory regression to S1 was shorter in Group BB (272.27 ± 15.39) when compared with Group BD (398.1 ± 6.50). It was statistically significant (p value = 0.048 < 0.05). There was a delay in sensory regression of approximately 1/3 times (30%) in Group **BD** comparing to Group BB.



HAEMODYNAMIC VARIABLES

Table 8: Mean arterial Pressure

Time Interval	BB Group (Mean ± SD)	BD Group (Mean ± SD)	P value
0 min	81.23 ± 10.45	80.17 ± 10.45	0.963
3 min	80.57 ± 13.35	80.90 ± 10.47	0.089
5 min	75.63 ± 14.47	80.33 ± 13.79	0.854
10 min	78.60 ± 13.71	83.20 ± 12.63	0.897
15 min	75.07 ± 11.96	78.97 ± 12.75	0.337
20 min	81.17 ± 13.09	79.53 ± 13.21	0.780
25 min	79.60 ± 10.83	79.60 ± 10.61	0.958
30 min	74.50 ± 10.86	76.97 ± 11.53	0.406
35 min	82.13 ± 12.96	83.47 ± 11.56	0.222
40 min	77.60 ± 10.93	76.43 ± 11.08	0.663
45 min	78.43 ± 11.50	77.57 ± 12.10	0.503

The mean arterial pressure was monitored from preoperative basal to 45th minute of the procedure (11 intervals). None of the intervals had statistical significance.

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DISCUSSION

Subarachnoid block with bupivacaine has been most extensively used for lower abdominal surgeries because of its simplicity, speed, reliability and minimal exposure to depressant drugs. However, a single intrathecal injection of bupivacaine alone provides analgesia for only 2 – 2.5 hours. Most patients require further analgesia during post operative period.

This double blinded, prospective, randomised study was conducted in Thanjavur medical college, Thanjavur with an aim to compare the effects of intrathecal Dexmedetomidine and Buprenorphine as an adjuvant to 0.5% hyperbaric bupivacaine.

The study included 60 patients belonging to the age group of 18-60 years of both sexes of ASA grade 1 and 2 scheduled to undergo elective lowerabdominal surgeries.

One of the study drugs, Buprenorphine, a highly lipophilic and centrally acting partial opioid agonist has rapid onset of action following intrathecal administration. It has been found recently that prolonged duration of action of buprenorphine is due to its local anaesthetic action [12]. The lesser side effectsin the post-operative period were due to its high lipid solubility [13].

Because of its high lipophilic nature, it diffuses quickly into the neural tissueand decreases the chance of rostral spread.

Another drug in the study, Dexmedetomidine which is a specific α2 adrenergic agonist, being used in recent times as an additive to intrathecal hyperbaric bupivacaine to prolong the quality and duration of analgesia. The mechanism for the prolongation of the duration of sensory and motor blockade produced by local anaesthetic is *not clearly known* [14]. It is attributed that α 2 adrenergic agonist (Dexmedetomidine) acts by binding to post synaptic dorsal horn neurons and to the C- fibres in the pre synaptic region. The prolonged analgesic action of intrathecal α2 agonist is by decreasing the release of C- fibres neurotransmitters and by causing hyperpolarisation of neurons in the post synaptic dorsal horn [15].

Even though there are lot of adjuvants, the above mentioned two adjuvants were considered for this study because there were only very few studies in the literature comparing the benefits and side effects of buprenorphine and dexmedetomidine as an adjuvants to bupivacaine for lower abdominal surgeries. Also, they are pharmacologically different drugs but their effects are similar in terms of hemodynamic stability, onset of sensory and motor block and adverse effects [16].

But these two drugs differ in the clinical effects especially in the duration of sensory and motor block, sensory regression and degree of sedation[27] .

Kanazi GE et al [17] have used 3 µg dexmedetomidine in their study and said to have comparable equipotent effect with clonidine. Hala EA Eid et al [18] studied the effects of dexmedetomidine on a dose related manner (control, 10 µg and 15µg) and confirmed the prolongation of duration of analgesia. Many studies have chosen 5µg of dexmedetomidine as an additive to intrathecal hyperbaric bupivacaine and proven efficacy[9]. Hence in our study we chose 5µg dexmedetomidine as an additive to hyperbaric bupivacaine.

Few studies have been conducted with a higher dosage of buprenorphine. Capogna et al [11], Mahima gupta et al [16] and sapkal Praveen S et al [19], have chosen 60µg of

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buprenorphine as an additive to intrathecal bupivacaine and showed to have a significant prolonged duration of analgesia along with nausea and vomiting that were not statistically significant.

Mahima gupta et al[16] also shown the duration of sensory blockade was 289.6 minutes in buprenorphine group and 493.6 minutes in dexmedetomidine group.

In this study, 75µg of buprenorphine was used instead of 60µg to evaluate whether the increased dosage of 15µg buprenorphine would help in further prolongation of duration of analgesia with a minimal side effects (PONV).

The results of the clinical study are discussed under the following headings.

Onset of sensory and motor block

Duration of sensory block

Duration of motor block

Time for sensory regression to S1

Hemodynamic stability and Adverse effects

ONSET OF SENSORY AND MOTOR BLOCK

The mean onset of sensory block in buprenorphine group was 3.47 minutes whereas in dexmedetomidine group it was 2.57 minutes. It was not statistically significant.

The mean onset of motor block in buprenorphine group was 3.83 minutes whereas in dexmedetomidine group, 4.13 minutes. It was not statistically significant.

Though the values of onset of motor blockade is similar to ***Mahima guptaet al***[27] and others, the onset of sensory blockade of dexmedetomidine group was clinically faster than buprenorphine group in our study which could not be explained.

DURATION OF ANALGESIA

Duration of analgesia was taken from the time of intrathecal injection of drugs to the first supplementation of rescue analgesic when patient complained of pain. In our study, the mean duration of analgesia was 332 minutes in buprenorphine group and 502.13 minutes in dexmedetomidine group.

The duration of analgesia in the Buprenorpine Group was 332 minutes whereas in the study conducted by Mahima gupta et al[16] it was 289.66 ±68.94. The prolongation of duration in our study could be explained by the dosage difference of buprenorphine (75 µg **Vs** 60µg). But the mean duration of analgesia in the studies conducted by Shaikh and Kiran et al[8] and Capogna et al [11]was 475 minutes and 430 minutes respectively which is very high than our study. This gross difference might be explained by the geriatric group of patients in Capogna et al and lower limb surgeries included in Safiya et al as noted by Mahima gupta et al.

The duration of analgesia in the dexmedetomidine group in the study conducted by Mahima gupta et al[16] was 493 minutes and the study conducted by Shah et al[14] was 474 minutes. The duration of analgesia was significantly prolonged in the study done by Rajni Gupta et al[9] (478 minutes). In our study, the mean duration of analgesia was 502.13 minutes in dexmedetomidine group which was similar to above mentioned studies. Also, the study done by Eid et at al[20] showed that duration of analgesia with dexmedetomidine Group was proportional to its dose.

In this study, Dexmedetomidine group had prolonged duration of analgesia compared to Buprenorphine group which was 51% higher than the later. Mahima Gupta et al [16] have shown similar results. The prolonged analgesic action of intrathecal α2 agonist is by decreasing the release of C-fibres neurotransmitters and by causing hyperpolarisation of

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neurons in thepost synaptic dorsal horn.

DURATION OF MOTOR BLOCK

The duration of motor block was taken from time of intrathecal drug administration to the time taken to attain modified bromage 3. The mean duration of motor block in Buprenorpine group was 298.6 minutes and indexmedetomidine group was 432.33 minutes (p value 0.00).

This was similar with the study conducted by Mahima gupta et al [16] **,** where the duration of motor block in *dexmedetomidine group* was 413.4 minutes and the study conducted by Rajni Gupta et al[9] **,** where the duration of motor block was 421 minutes.

The mean duration of motor block in *buprenorphine group* is 298.6 minutes, whereas the duration of motor block in Mahima gupta et al [16] study was 205.17 minutes which is significantly lower than our study. This could be explained by the increased dosage used in our study.

In our study itself, motor blockade in dexmedetomidine group was about **45%** prolonged than Buprenorpine group. Such a prolongation of motor blockade may not be liked by many patients who have undergone surgeries that would end by one hour. In this perspective, Buprenorphine would be a better adjuvant. Also, the duration of 'pure' sensory blockade (after the wear of motor blockade effect) in dexmedetomidine group was twice that of buprenorphine group (70 **Vs** 34 minutes). Still, Dexmedetomidine is a better drug as it would spare the rescue analgesic requirements.

CONCLUSION

The onsets of sensory and motor blockades were not statistically significance between the groups. The duration of both sensory and motor blockades were prolonged in *dexmedetomidine* group compared to buprenorphine group with the best statistical significance. Both groups had stable and comparable hemodynamics during the study.

Compared to buprenorphine, intrathecal administration of dexmedetomidine as additive to hyperbaric bupivacaine was associated with fewer side effects. The degree of sedation was better in the dexmedetomidine groupwhen compared to buprenorphine group.

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