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ORIGINAL RESEARCH

Comparative study of analgesic efficacy, hemodynamic stability, and adverse effects of injection Buprenorphine versus Dexmedetomidine as adjuvant with 0.5% hyperbaric bupivacaine in patients undergoing moderate duration surgeries

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ABSTRACT

Background: Intrathecal opioids are the gold standard for the treatment of post-operative pain with Buprenorphine adjudged as the most effective due its potent and prolonged effects. However, over the years it is losing popularity due to dose dependant side effects such as pruritus, nausea, vomiting and the most feared risk of delayed respiratory depression. Hence the search for an agent which can provide potent postoperative analgesia as comparable to morphine without its side effects still continues.

Aim & Objective: study intrathecal Dexmedetomidine 10mcg and Buprenorphine 75mcg used as adjuvant to 0.5% hyperbaric Bupivacaine to study- The onset of sensory block., Time of achieving highest level of sensory block. The onset of motor block. The Hemodynamic Effects. The Adverse Effects. Methods: Randomized clinical trial, Study setting: Anaesthesia Department of tertiary care centre. Study duration: from April 2021 to March 2022 Study population: All patients with cataract requiring surgery admitted in tertiary care center. Sample size: 100. Results: Dexmedetomidine group- 4 (8%) patients were less than 20 years of age, 34 (68%) patients were between 20-40 years of age, 12 (24%) patients were between 41-58 years of age. Buprenorphine group- 1(2%) patient was less than 20 years of age ,34(68%) were between 20-40 years of age, 15(30%) were between 41-58 years of age. 47(94%) patients in Dexmedetomidine group were males and 3(6%) were females.38(76%) patients in Buprenorphine group were males and 12(24%) were females. Dexmedetomidine group 47(94%) patients were ASA 1 grade whereas 3(6%) patients were ASA 2 grade. Buprenorphine group 43(86%) patients were ASA 1 grade whereas 7(14%) patients were ASA 2 grade. Dexmedetomidine group was earlier with mean 3.06 ± 0.45 min whereas 3.46 ± 0.59 min in buprenorphine group, P value 0.0002492 which was significant as it was less than 0.05. so onset of sensory block was significantly earlier in Dexmedetomidine group than Buprenorphine group. No significant difference was seen in the distribution of maximum sensory level among patients in both the group as observed p value is 0.532 which was >0.05. From 10 min onwards, Hollmen score was 3 among both group which denotes no perception of pinprick 15min after giving spinal anaesthesia. Conclusions: Time of onset of sensory block and motor block was earlier in Dexmedetomidine group than the Buprenorphine group. Duration of sensory block and motor block was prolonged in Dexmedetomidine group than the Buprenorphine group. Two segment

regression of sensory level was significantly later among Dexmedetomidine group than Buprenorphine group.

Keywords: Dexmedetomidine, Buprenorphine, sensory block, motor block, Hollmen score

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INTRODUCTION

Post-operative pain management is one of the main challenges for anaesthesiologists and even with the help of multimodal analgesia technique, patients still remain undertreated.[1] Since no single modality for the post operative pain relief has proven to be effective without side effects, we continue to explore modern strategies with new drug combinations. The addition of different adjuvants intrathecally is an attractive analgesic strategy due to simple and quick technique with low risk of failure and infection.

Anaesthesiologists have added multiple adjuvants drugs such as epinephrine, opioids, alpha2 adrenergic receptor (AR) agonists and many other local anaesthetic agents. Intrathecal opioids are the gold standard for the treatment of post-operative pain with Buprenorphine adjudged as the most effective due its potent and prolonged effects. However, over the years it is losing popularity due to dose dependant side effects such as pruritus, nausea, vomiting and the most feared risk of delayed respiratory depression.[2] Hence the search for an agents which can provide potent postoperative analgesia as comparable to morphine without its side effects still continues.[3]

Dexmedetomidine is highly selective alpha2AR agonist which possesses sedative, analgesic and sympatholytic properties and gives prolonged analgesia when used intrathecally without respiratory depression. Intrathecal dexmedetomidine has been found to be ten times more potent analgesic and anaesthetic as compared to intrathecal clonidine and five times more potent than opioids like intrathecal fentanyl[4]

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.

AIM AND OBJECTIVES:

Comparative study of analgesic efficacy, hemodynamic stability, and adverse effects of injection buprenorphine versus dexmedetomidine as adjuvant with 0.5% hyperbaric bupivacaine in patients undergoing moderate duration surgeries.

OBJECTIVES:

In this study intrathecal Dexmedetomidine 10mcg and Buprenorphine 75mcg used as adjuvant to 0.5% hyperbaric Bupivacaine to study-

1.The onset of sensory block.
2. Time of achieving highest level of sensory block.
3.The onset of motor block
4.The Hemodynamic Effects.
5. The Adverse Effects

METHODOLOGY

Study design: Randomized clinical trial. **Study setting:** Anaesthesia department of tertiary care centre.**Study duration:** …..

Study population: All patients requiring spinal anaesthesia admitted in tertiary care center

Sample size: 100 patients (50 patients received 3ml injection 0.5% heavy bupivacaine with 10mcg injection Dexmedetomidine and 50 patients received 3ml injection 0.5% heavy bupivacaine with 75mcg injection Buprenorphine as additive intrathecally.

Inclusion criteria:

Age: 18 to 58 years

ASA Grade: I,II

Surgeries less than 3 hours duration

Either sex

Exclusion criteria:

Following patients were excluded from the study:

Patient's refusal.,Patients allergic to study drug or any other substance, ASA Grade 3 and 4,Age less than 18yrs and more than 58yrs. Pregnancy, Infection at the site of sub-arachanoid block, Focal neurological deficit, Difficult airway, Preexisting peripheral neuropathy. Spine deformity, Patients having coagulation disorders.

STUDY PROCEDURE:

Anaesthetic techniques:

After confirming adequate NBM status and valid informed consent patient were shifted to operation table. Electrocardiogram, Pulse oximetry, and Noninvasive blood pressure were attached and baseline reading (0 reading) of vital parameters were recorded. This was followed by intravenous cannulation using 18G / 20G cannula. Preloading were started using Ringer Lactate solution @8 to 10ml/kg. The patient were assigned to one of the following groups using randomisation chart.

The study solutions were prepared in a 5 ml syringe. Proposed amount of Group B(Buprenorphine) was added by using insulin syringe. Final volume of solution was made 3.1ml by adding normal saline as required. Proposed amount of Group D (Dexmedetomidine) was added by using insulin syringe. Final volume of solution was made 3.1 ml.

Under all aseptic precautions subarachnoid block was administered at the L_{2-3} or L_{3-4} vertebral level using 25-gauge /23 guage Quincke's spinal needle by midline approach with patients in the sitting position. Rate of injection was kept constant

0.2 ml/sec using a stop watch. Patients was made supine following the block immediately.

The anaesthesiologist who was performing the block and record the parameters was blind regarding the study group to which patient belongs. The onset and duration of sensory block, highest level of sensory block, time to reach the highest dermatomal level of sensory block, 2 segment regression of spinal block, motor block onset, time to achieve motor block of modified Bromage score 3, time to complete recovery of motor block were recorded. The sensory level was assessed according to **Hollmen scale**[40]

METHOD OF COLLECTION OF DATA:

Ethical Clearance: Ethical clearance was obtained from institutional ethics committee. Informed consent was obtained from study subjects after explaining study procedure in local language. Predesigned and pretested case record form was used as a tool for data collection. All patients fulfilling the inclusion criteria were subjected to detailed history taking regarding symptoms and duration of disease. Data was collected about sociodemographic characteristics of study subjects like age, sex, address, occupation education status and socioeconomic status. Also data regarding past medical history and comorbid conditions like

diabetes and hypertension was collected in case record form. A careful and detailed ocular examination as well as clinical examination was undertaken.

STATISTICAL ANALYSIS:

Data was entered in windows excel format and presented with the help of frequency and percentage tables. Association among the study groups is assessed with the help of chi-square test using OpenEPI statistical software version 3.01. P value less than 0.05 was taken as significant. Graphical representation is done in MS excel 2010.

OBSERVATIONS AND RESULTS

The observations and results of the present study are as follows

Table A: showing Maximum level of sensory block comparison among Dexmedetomidine and Buprenorphine group-

Maximum sensory level	Dexmedetomidine Group		Buprenorphine Group	
	Frequency (n=50)	Percentage (%)	Frequency (n=50)	Percentage (%)
T6	7	14	9	18
T8	42	84	41	82
T10	1	2	0	0
P Value = 0.5320				

Out of 50 patients 7 (14%) patients in Dexmedetomidine group achieved T6 level, 42(84%) patients achieved T8 level ,1(2%) patient achieved T10 level.

Out of 50 patients 9(18%) patients among buprenorphine group achieved T6 level, 41(82%) patients achieved T8 level ,0 patient achieved t10 level.

No significant difference was seen in the distribution of maximum sensory level among patients in both the group as observed p value is 0.532 which was >0.05.

Table B: showing time required to achieve maximum sensory level comparison among Dexmedetomidine and Buprenorphine group

Time required to achieve maximum sensory level(min.sec)	Dexmedetomidine Group		Buprenorphine Group	
	Frequency (n=50)	Percentage (%)	Frequency (n=50)	Percentage (%)
$\leq$ 4	18	36	14	28
> 4	32	64	36	72
Mean $\pm$ SD	4.44 $\pm$ 0.5		5.76 $\pm$ 1.8	
	P Value = 0.000005877			

Time for maximum sensory block was earlier among Dexmedetomidine group with mean 4.44 ± 0.5 min whereas 5.76 ± 1.8 min in buprenorphine group, P value 0.000005 which was significant as it was less than 0.05.

Table C: showing comparison of onset of motor block among Dexmedetomidine and buprenorphine group

onset of motor block(min.sec)	Dexmedetomidine Group		Buprenorphine Group	
	Frequency (n=50)	Percentage (%)	Frequency (n=50)	Percentage (%)
≤ 4	16	32	37	74
> 4	34	68	13	26
Mean ± SD	4.12 ± 0.43		4.01 ± 0.42	
	P Value = 0.1987			

Onset of motor block among Dexmedetomidine group was 4.12 ± 0.43 min whereas 4.01 ± 0.42 min in buprenorphine group with P value 0.1987 which was not statistically significant.

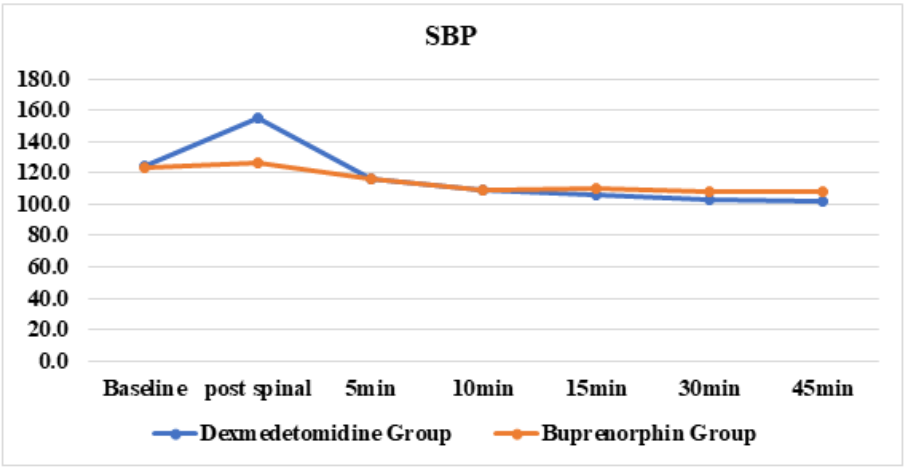
Table D: showing Comparison of Mean Heart rate among Dexmedetomidine and buprenorphine group-

Heart Rate	Dexmedetomidine Group		Buprenorphine Group		P Value
	Mean	SD	Mean	SD	
Baseline	90.2	6.8	81.8	9.0	0.000000927
post spinal	96.1	7.0	85.1	9.4	0.0000001
5min	83.9	6.4	76.8	13.0	0.0009040
10min	78.0	5.3	75.3	7.3	0.03711
15min	73.9	5.2	73.6	7.5	0.8167
30min	71.8	5.0	71.7	7.8	0.9393
45min	70.6	4.8	72.6	8.1	0.1370

At post-spinal time of study mean of heart rate among Dexmedetomidine group was 96.1 ±7.0 and 85.1 ± 9.4 in buprenorphine group, with P value 0.000001 which was significant.

5 min after giving spinal, heart rate was significantly higher in buprenorphine group mean of heart rate among fentanyl group was 72.45 ± 9.56 and 81.96 ± 13.85 in buprenorphine group, with P value 0.0009 which was significant.

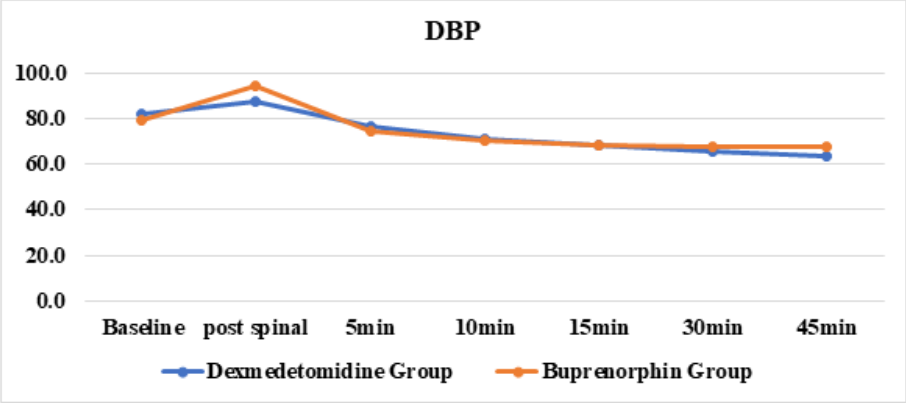
10 min onwards in rest of the study there was no significant difference in heart rate among both groups.



Graph 1: Showing mean systolic blood pressure

Systolic blood pressure was significantly higher among patients in Buprenorphine group at 15 min, 30 min and 45 mins.

No significant difference in the systolic blood pressure was seen among patients in both the group in rest of the study period.



Graph 2: Showing mean Diastolic blood pressure

Diastolic blood pressure was significantly higher among patients in buprenorphine group at 30 min and 45 min.

No significant difference in the diastolic blood pressure was seen among patients in both the group in rest of the study period.

Table E: showing Comparison of Mean arterial pressure (MAP) among Dexmedetomidine and buprenorphine group-

MAP	Dexmedetomidine Group		Buprenorphine Group		P Value
	Mean	SD	Mean	SD	
Baseline	96.5	4.0	94.1	7.1	0.04062
post spinal	102.1	4.3	96.5	8.4	0.00007547
5min	90.3	5.2	89.1	6.6	0.3152
10min	84.0	3.5	84.5	5.9	0.6077
15min	81.2	3.1	82.6	5.3	0.1109
30min	78.3	3.4	81.5	4.4	0.00009956
45min	76.8	3.2	81.6	4.4	0.0000001

5,10,15 min after giving spinal, there was no significant difference among both groups.

30 min after giving spinal there was significantly higher MAP among buprenorphine group with p value 0.000099.

45 min after giving spinal DBP showed significant difference with buprenorphine group showing higher MAP than Dexmedetomidine group with P value 0.0000001.

no significant difference was seen among both group till rest of study time.

Table F: showing Adverse events reported among Dexmedetomidine and Buprenorphine group-

Adverse Reactions	Dexmedetomidine Group		Buprenorphine Group	
	Frequency (n=50)	Percentage (%)	Frequency (n=50)	Percentage (%)
Nausea	0	0	4	8
Vomiting	0	0	1	2
Shivering	0	0	5	10
No Reaction	50	100	40	80
P value = 0.01114				

Number of adverse events was significantly higher among buprenorphine group than with Dexmedetomidine group with P value was 0.01114 which was significant.

DISCUSSION

Subarachnoid block with bupivacaine has been most extensively used 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.

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.[6] The lesser side effects in the post-operative period were due to its high lipid solubility.[7] Because of its high lipophilic nature, it diffuses quickly into the neural tissue and 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.[8] 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[9]

Hala EA Eid et al[10] studied the effects of dexmedetomidine in 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. Hence in our study we chose 10µg dexmedetomidine as an additive to hyperbaric bupivacaine for determining whether increased dose increases Duration of analgesia.

Few studies have been conducted with a higher dosage of buprenorphine. Capogna et al[11], showed to have a significant prolonged duration of analgesia along with nausea and vomiting that were not statistically significant. In our study we chose to use 75 ug buprenorphine for determining whether increased dose increases duration of analgesia with minimal side effects.

The total number of patients enrolled in this study was 100 with Dexmedetomidine(10mcg) or Buprenorphine(75mcg) administered intrathecally with 0.5%Bupivacaine(3ml) in 50 patients each respectively for moderate duration surgeries(<3hrs). All the subjects included in the study volunteered after proper consent. The study was conducted after obtaining clearance from the ethical committee of the institute. Demography (age, sex, weight, ASA grading) was comparable in Dexmedetomidine and Buprenorphine groups. There was no statistically significant difference amongst demography in our study.

Onset of sensory block among Dexmedetomidine group was earlier with mean 3.06 ± 0.45 min whereas 3.46 ± 0.59 min in buprenorphine group with P value 0.0002492 which was significant. Xiaofei Qi et al.[12] have conducted study in 2016 for comparison of inj. Dexmedetomidine and inj. Morphine where they observed similar results of Quicker onset time for sensory Block. The dose of Dexmedetomidine in their study(5ug) was comparable with our study (10ug).

In our study Out of 50 patients 7 (14%) patients in Dexmedetomidine group achieved T6 level, 42(84%) patients achieved T8 level ,1(2%) patient achieved T10 level whereas Out of 50 patients 9(18%) patients among buprenorphine group achieved T6 level, 41(82%) patients achieved T8 level ,0 patient achieved T10 level which was not statistically significant (P value 0.532).

In our study Two segment regression among Dexmedetomidine group was later with mean 239.9 ± 13.7 min whereas 139.2 ± 14.4 min in buprenorphine group, P value 0.0000001 which was significant as it was less than 0.05. Similarly in a study conducted by Vidhi

Mahendru et al.[13] in 2013 for comparison of the onset, duration of sensory and motor block, hemodynamic effects, postoperative analgesia, and adverse effects of dexmedetomidine (5mcg), clonidine (30mcg) and fentanyl (25 mcg) used intrathecally with hyperbaric 0.5% bupivacaine for spinal anaesthesia, they observed that Two segment Regression was later in Dexmedetomidine group as compared to other groups as observed in our study.

In our study, Total duration of sensory block among dexmedetomidine group was higher with mean 504.4 ± 30.68 min whereas 374.4 ± 20.7 min in buprenorphine group, P value 0.0000001 which was significant. Similarly in a study conducted by Amar Prakash Kataria et al.[14] observed that total duration of sensory block was higher in Dexmedetomidine+ levobupivacaine(340.20 ± 11.78 min) group compared to normal saline + levobupivacaine(199.50 ± 7.96 min)group.

In our study Onset of motor block among Dexmedetomidine group was 4.12 ± 0.43 min whereas 4.01 ± 0.42 min in buprenorphine group with P value 0.1987 which was not statistically significant.

In our study Total duration of motor block was higher among Dexmedetomidine group with mean 444.5 ± 19.7 min whereas 274.1 ± 12.8 min in buprenorphine group with P value 0.0000001 which was significant. This was similar with the study conducted by Mahima Gupta, S.Shailaja, K.Sudhir Hegde[15] where the duration of motor block in dexmedetomidine group was 413.4 minutes.

Number of adverse events was significantly higher among buprenorphine group than with Dexmedetomidine group with P value was 0.01114 which was significant. The incidence of nausea and vomiting were more in buprenorphine group as compared to dexmedetomidine group which is similar to the study conducted by in Mahima Gupta, S.Shailaja, K.Sudhir Hegde.[15] Capogna et al[11] also observed more number of nausea and vomiting in buprenorphine group. Similar observations were seen by Sapkal pravin S et al.[16]

CONCLUSION

In our study we compared Inj. Dexmedetomidine 10ug and Inj. Buprenorphine 75ug as additive to 3ml Inj. Bupivacaine 0.5% in moderate duration surgeries in spinal anaesthesia for Moderate duration surgeries.

Following conclusions were drawn:

1. Time of onset of sensory block and motor block was earlier in Dexmedetomidine group than the Buprenorphine group.
2. Duration of sensory block and motor block was prolonged in Dexmedetomidine group than the Buprenorphine group.
3. Two segment regression of sensory level was significantly later among Dexmedetomidine group than Buprenorphine group.
4. There was high statistically significant difference in Duration of analgesia when both groups compared with Dexmedetomidine group showing more prolonged duration of analgesia.
5. Some Adverse effects were seen among Buprenorphine group as compared to Dexmedetomidine group which were not severe.

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