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RESEARCH ARTICLE
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COMPARISON OF EFFECT OF DEXMEDETOMIDINE VS. BUPRENORPHINE AS ADJUVANTS TO INTRATHECAL 0.5 % HYPERBARIC BUPIVACAINE IN LOWER LIMB ORTHOPAEDIC SURGERIES IN GOVERNMENT T.D. MEDICAL COLLEGE HOSPITAL ALAPPUZHA

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ABSTRACT

Background: Various adjuvants have been used with bupivacaine in spinal anaesthesia, the advantages being ability to use a lower dose of local anaesthetic, with better hemodynamic stability and prolongation of intraoperative and postoperative analgesia.

Objective: To compare effect of Dexmedetomidine vs. Buprenorphine as adjuvants to intrathecal 0.5 % hyperbaric bupivacaine in lower limb orthopedic surgeries based on duration of analgesia, onset of sensory & motor block, duration of sensory & motor block and side effects if any.

Methods: This study was done among patients in the age group of 18-60 years, belonging to ASA 1& 2, who underwent elective lower limb orthopaedic surgeries. Both the groups of patients were comparable with regard to age, height and weight. They were allocated into two groups of 28 patients each by using computer generated random sequence. Group A received 2.8ml of 0.5% hyperbaric bupivacaine and 0.2ml (5mcg) dexmedetomidine. Group B receive 2.8ml of 0.5% hyperbaric bupivacaine and 0.2ml(60mcg) buprenorphine

Result: The mean time of onset of analgesia in dexmedetomidine group was1.06 ± 0.13 min, which was significantly faster than Buprenorphine group 1.39 ± 0.13min ($P<0.001$). The mean duration of analgesia in dexmedetomidine group was 574.71 ± 25.08 min as compared to buprenorphine group which was 404.14 ± 13.28 min, the difference being statistically significant ($p< 0.001$). Mean onset of motor block in dexmedetomidine group was 1.27 ± 0.14 min and in buprenorphine group was 1.79± 0.14 min ($p< 0.001$). Mean duration of motor blockade in dexmedetomidine group was 387.96 ± 17.22 min and in buprenorphine group was 268.93 ± 13.21 min ($p< 0.001$). In dexmedetomidine group, time to two segment regression was 137.89 ± 18.61min which was significantly prolonged than buprenorphine group 111.96 ± 7.2min ($p< 0.001$).

Conclusion: Dexmedetomidine seems to be a better alternative to buprenorphine as adjuvant in spinal anaesthesia as it has faster onset of sensory and motor block,prolonged duration of analgesia and motor blockade along with fewer side effects.

Keywords: Spinal anaesthesia, Dexmedetomidine, Buprenorphine, Bupivacaine

INTRODUCTION

Spinal anaesthesia is the most commonly used technique for lower limb orthopaedic surgeries as it is reliable, easy to administer, safe and economical. Bupivacaine 0.5% heavy is the most commonly used local anaesthetic. Various adjuvants have been used with bupivacaine in spinal anaesthesia, the advantages being ability to use a lower dose of local anesthetic, with better hemodynamic stability and prolongation of intraoperative and postoperative analgesia[1]. These adjuvants include opioids like Morphine, Fentanyl and Sufentanyl and non opioids like Ketamine, Midazolam, Neostigmine, Clonidine, dexmedetomidine and magnesium sulphate[2].

Buprenorphine, a thebaine derivative, is a mixed agonist and antagonist narcotic with high affinity at both mu and kappa opiate receptors. Its weak antagonistic effect prevents its addiction and physical dependence. It is an effective analgesic, similar to morphine, in nearly all clinical situations[3]. Buprenorphine is highly lipophilic in nature, which remains attached to spinal opioid receptors providing longer duration. It augments the effects of local anaesthetics and also decreases the requirement of postoperative analgesics .

Dexmedetomidine a novel drug is being used in anaesthetic practice for its sedative, anxiolytic, analgesic, neuroprotective and anaesthetic sparing effects. It is a highly selective α2 agonist and in neuraxial anaesthesia, it mediates its analgesic effects via spinal α2 receptors by depressing the release of C fiber neurotransmitter and hyperpolarization of post-synaptic dorsal neurons[4]. It provides a good quality of intraoperative and post operative analgesia with minimal side effects.

There are many studies comparing these two drugs as adjuvants in spinal anaesthesia. comparing these two drugs dexmedetomidine vs. buprenorphine as adjuvants to bupivacaine for lower limb orthopeadic surgeries. So, we decided to conduct a study in order to find the drug amongst them with maximum duration of action and least incidence of side effects.

OBJECTIVES

- **Primary objective:** To compare efficacy of dexmedetomidine and buprenorphine as adjuvant based on duration of analgesia
- **Secondary objectives**

a) To assess the onset of sensory & motor block
b) duration of sensory & motor block
c) side effects if any

MATERIALS & METHODS

This observational study was conducted in Government T.D. Medical College Alappuzha, from June 2021 to December 2022. Ethical clearance was obtained from the Institutional Ethics Committee (IEC), Government. T.D. Medical College, Alappuzha (EC 59/2021, Date 22/04/21). Informed consent was obtained from all the participants.

Inclusion Criteria

Patients undergoing elective lower limb orthopaedic surgeries under spinal anaesthesia, who gave consent to take part in this study, Age between 18 and 60 years, Weight less than 100kg, Height between 145 cm to 170cm, ASA 1 & 2

Exclusion Criteria

ASA physical status Grade III and IV, Patients with sinus bradycardia(Heart rate<50/min)

Sample Size Estimation

Sample size was estimated by using the difference in mean duration of analgesia between hyperbaric bupivacaine plus buprenorphine group and hyperbaric bupivacaine plus dexmedetomidine group from the study "Comparison of dexmedetomidine and buprenorphine as an adjuvant to bupivacaine during spinal anaesthesia for tibial interlocking nailing surgeries" by Amitha S et al(4), as 210+/-22.4 min and 240+/-30.2min. Using these values at 99% confidence limit and 90% power sample size of 25 was obtained in each group by using the below mentioned formula and Med calc sample size software. With 10% non response sample size of 25+2.5~ 28 cases will be included in each group. by substituting the values in the formula:
$(Z\ \alpha/2 + Z\beta)\ 2\ X\ (SD)^{2} \times 2/(d)2$,

Sample size for comparing two means
Input data
Confidence interval (2-sided) - 99%
Power - 90%
Difference of means - 30
Standard deviation in group 1 - 22.4
Standard deviation in group 2 - 30.2
Ratio of sample size (group1/group2) - 1
$=2 \times (22.4+30.2)^2\ (2.58+1.28)^2/(30)^2$
=23 cases (manual)
=25 cases (software) it consider decimals as well
10% error, 25+2.5 ~ 28 cases in each group
Total sample size = 56

Method of data collection

Participants were enrolled in the study according to inclusion and exclusion criteria. After obtaining informed and written consent from the patients, the participants were subjected to a detailed history, a clinical examination, and relevant blood investigations. Patients were allocated in to 2 study groups of 28 patients each by computer generated Random Sequence.

Group A: Received 2.8ml of 0.5% hyperbaric bupivacaine and 0.2ml (5mcg) dexmedetomidine.

Group B: Received 2.8ml of 0.5% hyperbaric bupivacaine and 0.2ml(60mcg) buprenorphine.
The drug was prepared by a resident anaesthesiologist. Consultant anaesthesiologist doing the procedure and the investigator were blinded to the nature of the drug given and the investigator observed the effects.

- Systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate were recorded every 5 min .
- Time for onset of sensory block, onset of motor block, duration of analgesia, duration of sensory and motor block and occurrence of side effects were noted.

Onset of analgesia was assessed as time interval from completion of spinal injection to loss of pinprick sensation at T 10 and onset of motor block as the time interval from completion of spinal injection to motor blockade (Bromage scale -2).
Duration of sensory block - After surgery, dermatomal level was assessed every half hour until the point of 2 segment regression of sensory level. Duration of analgesia was assessed as the time interval from completion of spinal injection till the patient complained of pain (VAS score≥4) and duration of motor blockade as the time interval from completion of spinal injection till the patient attained complete motor recovery (Bromage scale -0).

Statistical analysis

Data was entered into Microsoft excel data sheet and was analysed. Categorical data was represented in the form of Frequencies and proportions. Chi square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test or Mann Whitney U test was used as test of significance to identify the mean difference between two quantitative variables and qualitative variables respectively. Graphical representation was done using bar diagram and line diagram. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS

The Demographic profile of the patients in each group was comparable with respect to mean age, gender distribution, weight, height and ASA physical status. The mean time of onset of analgesia in dexmedetomidine group was 1.06 ± 0.13 min, which was significantly faster than Buprenorphine group 1.39 ± 0.13min (P<0.001). The mean duration of analgesia in dexmedetomidine group was 574.71 ± 25.08 min as compared to buprenorphine group which was 404.14 ± 13.28 min ,the difference being statistically significant (p< 0.001). Mean onset of motor block in dexmedetomidine group was 1.27 ± 0.14 min and in buprenorphine group was 1.79 ± 0.14 min (p< 0.001). Mean duration of motor block in dexmedetomidine group was 387.96 ± 17.22 min and in buprenorphine group was 268.93 ± 13.21 min (p< 0.001). In dexmedetomidine group, time to two segment regression was 137.89 ± 18.61min which was significantly prolonged than buprenorphine group 111.96 ± 7.2min (p< 0.001). When comparing the side effects between dexmedetomidine group and buprenorphine group 4 patients in each group developed hypotension, incidence being 14.29% which was not statistically significant. So it was concluded that there was no significant difference in the incidence of hypotension between two groups. 2 patients in the dexmedetomidine group (7.14%) developed bradycardia . No patient in buprenorphine group developed bradycardia.

None of the patients in either group developed nausea or vomiting

	Group				**p value**
	Dexmedetomidine		**Buprenorphine**		
	Mean	SD	Mean	SD	
Age	37.18	10.34	37.79	9.66	0.821

Table 1: Mean Age comparison between two groups

	Group				
	Dexmedetomidine			**Buprenorphine**	
	Count		**%**	**Count**	**%**
	Female	4	14.29%	6	21.43%
Sex distribution	Male	24	85.71%	22	78.57%

Table 2: Sex Distribution between two groups

	Group				
	Dexmedetomidine			**Buprenorphine**	
	Count		**%**	**Count**	**%**
	ASA 1	23	82.14%	24	85.71%
ASA	ASA 2	5	17.86%	4	14.29 %

Table 3: ASA Distribution between two groups

	Group				p value
	Dexmedetomidine		Buprenorphine		
	Mean	SD	Mean	SD	
Weight	62.68	7.49	61.89	8.01	0.706

Table 4: Mean Weight comparison between two groups

	Group				p value
	Dexmedetomidine		Buprenorphine		
	Mean	SD	Mean	SD	
Height	165.04	3.58	164.96	4.91	0.951

Table 5: Mean Height comparison between two groups

	Group				p value
	Dexmedetomidine		Buprenorphine		
	Mean	SD	Mean	SD	
Duration of analgesia	574.71	25.08	404.14	13.28	< 0.001*

Table 6 : Mean Duration of analgesia comparison between two groups

Mean Duration of analgesia in Dexmedetomidine Group was 574.71 ± 25.08 and in Buprenorphine Group was 404.14 ± 13.28. There was a significant difference in mean Duration of analgesia comparison between two groups.

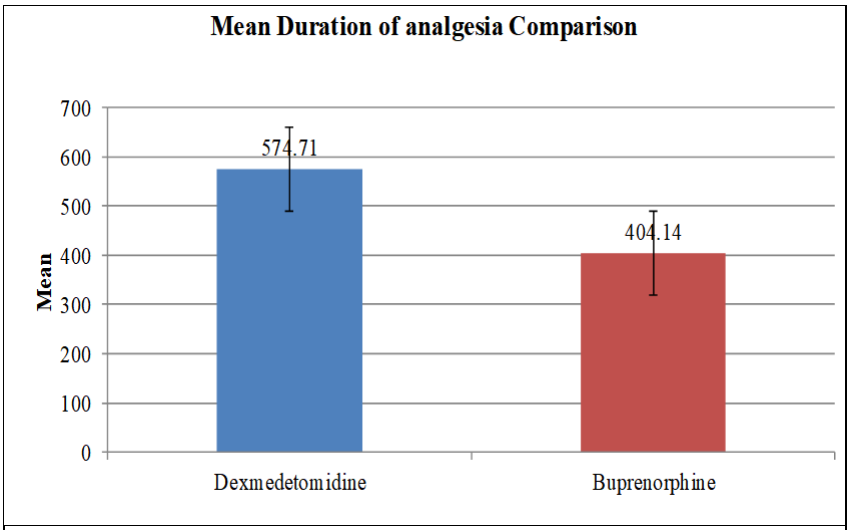

Figure 1

	Group				p value
	Dexmedetomidine		Buprenorphine		
	Mean	SD	Mean	SD	
Time to attain T10 level	1.06	0.13	1.39	0.13	< 0.001*

Table 7: Mean Time to attain T10 level comparison between two groups

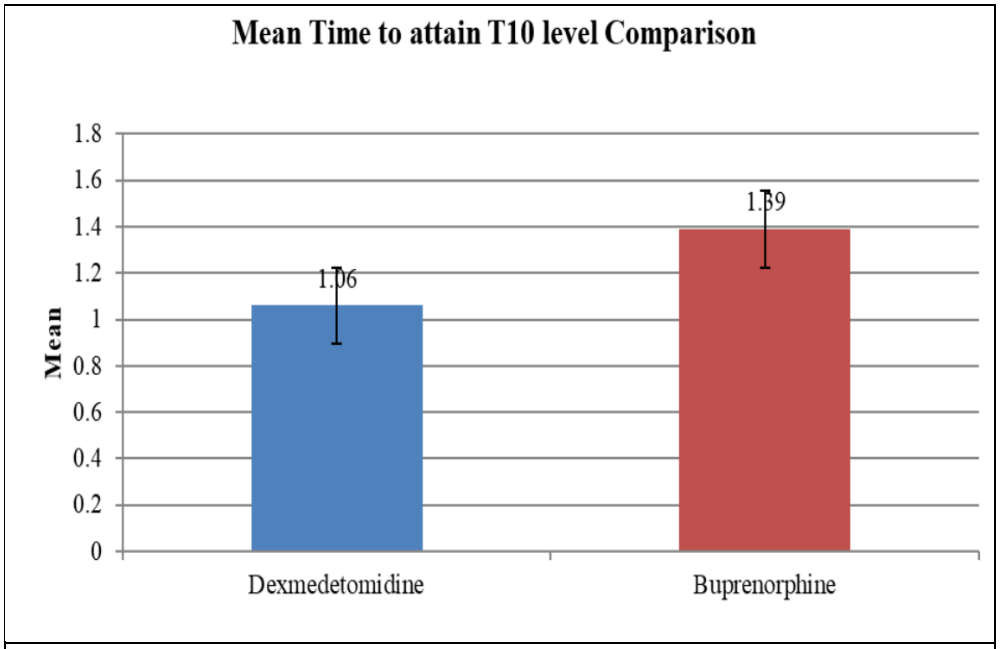

Figure 2

Mean Time to attain T10 level in Dexmedetomidine Group was 1.06 ± 0.13 and in Buprenorphine Group was 1.39 ± 0.13. There was a significant difference in mean Time to attain T10 level comparison between two groups.

	Group				**p value**
	Dexmedetomidine		**Buprenorphine**		
	Mean	**SD**	**Mean**	**SD**	
Time of onset of motor block	1.27	0.14	1.79	0.14	< 0.001*

Table 8: Mean Time of onset of motor block comparison between two groups

Mean Time of onset of motor block in Dexmedetomidine Group was 1.27 ± 0.14 and in Buprenorphine Group was 1.79 ± 0.14. There was a significant difference in mean Time of onset of motor block comparison between two groups.

	Group				**p value**
	Dexmedetomidine		**Buprenorphine**		
	Mean	SD	Mean	SD	
Duration of motor block	387.96	17.22	268.93	13.21	< 0.001*

Table 9: Mean Duration of motor block comparison between two groups

Mean Duration of motor block in Dexmedetomidine Group was 387.96 ± 17.22 and in Buprenorphine Group was 268.93 ± 13.21. There was a significant difference in mean Duration of motor block comparison between two groups.

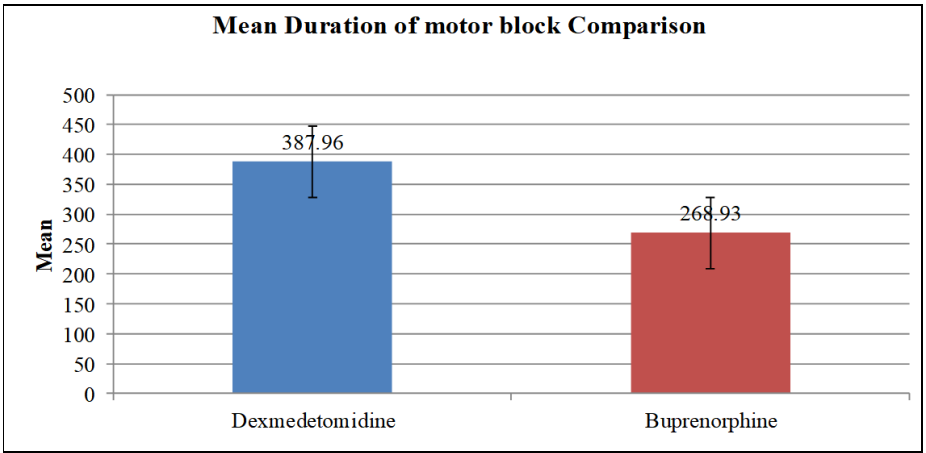

Figure 3

		Group				p value
		Dexmedetomidine		Buprenorphine		
		Count	Column N %	Count	Column N %	
Nausea	No	28	100.00%	28	100.00%	-
vomiting	No	28	100.00%	28	100.00%	-
hypotension	No	26	92.86%	24	85.71%	1.000
	Yes	2	7.14%	4	14.29%	
bradycardia	No	26	92.86%	28	100.00%	0.150
	Yes	2	7.14%	0	0.00%	

Table 10: Side Effects Distribution between two groups

There was no significant difference in Side Effects Distribution between two groups.

DISCUSSION

Literature search has shown that 60 µg buprenorphine is the most common dose used in spinal anaesthesia. Hence these doses of dexmedetomidine and buprenorphine respectively were selected in our study.The Demographic profile of our patients in each group was comparable with respect to mean age, gender, weight, height and ASA physical status. In our study, the mean time of onset of analgesia in dexmedetomidine group was 1.06 ± 0.13 min , which was significantly faster than Buprenorphine group 1.39 ± 0.13min (P<0.001). A study by Kannan et al,[5] and Amita et al,[4] showed similar results with dexmedetomidine having faster onset when compared to buprenorphine. Difference in onset time between our study and above studies may be due to the fact that our study was done in lower limb surgeries where T10 level was assessed. Other studies were done in lower abdominal surgeries where T8 level for assessment has been used. Mean onset of motor block in dexmedetomidine group was 1.27 ± 0.14 min and in buprenorphine group was 1.79 ± 0.14 min (p< 0.001). This is in accordance with study done by Deepa et al,[6] where they reported faster onset of motor block in dexmedetomidine group than in buprenorphine group. The time of onset is considerably faster in our study probably because Bromage scale 2 was taken as the onset of motor block, where as in the above study Bromage scale 3 was taken as a measure of motor block. Mean duration of motor block in dexmedetomidine group was 387.96 ± 17.22 min and in buprenorphine group was 268.93 ± 13.21 min (p< 0.001). Addition of dexmedetomidine prolongs the duration of motor block about 6 hours compared to buprenorphine which is about 4 hours. Our study had shown that mean duration of analgesia in dexmedetomidine group was 574.71 ± 25.08 min as compared to buprenorphine group which was 404.14 ± 13.28 min, the difference being statistically significant (p< 0.001) . These findings were similar to the study done by Gupta M et al, [7] Both of us have used similar doses of dexmedetomidine and buprenorphine. In their study duration of analgesia in dexmedetomidine group was 493.56±385.95 min and in buprenorphine group was

289.66 ±64.94min. Even though same doses of drugs were used, the difference in the duration of analgesia between this study and our study may be because the above study was conducted in lower abdominal surgeries where due to block regression patient might have experienced pain earlier. When comparing the side effects between dexmedetomidine group and buprenorphine group 4 patients in each group developed hypotension, incidence being 14.29% which was not statistically significant. It was concluded that there was no significant difference in the incidence of hypotension between two groups.

Two patients in the dexmedetomidine group (7.14%) developed bradycardia, which required treatment with Atropine. No patient in buprenorphine group developed bradycardia. None of the patients in either group developed nausea or vomiting. Shuyan Liu et.al,[8] in their meta analysis found that dexmedetomidine was associated with increased risk of transient bradycardia (RR = 1.59; 95% CI, 1.07-2.37; P = 0.022) and hypotension (RR = 1.40; 95% CI, 1.04-1.89; P = 0.026) but did not increase the incidence of postoperative nausea and vomiting (RR = 0.87; 95% CI, 0.62-1.24 P-0.45)

CONCLUSION

The addition of 5ug dexmedetomidine to 0.5% hyperbaric bupivacaine prolonged the duration of analgesia and motor blockade significantly more than addition of 60µg buprenorphine to 0.5% hyperbaric bupivacaine. The incidence of side effects such as hypotension, bradycardia are insignificant in both the groups, and none of the patients developed nausea and vomiting. So, from this study it can be concluded that dexmedetomidine seems to be a better alternative to buprenorphine in spinal anaesthesia as it has faster onset of sensory and motor block, prolonged duration of analgesia and motor blockade along with fewer side effects.

AUTHOR CONTRIBUTION

Dr. Aswathy M.S. - Concept and design of the work, Data collection, Data analysis and interpretation, drafting of the article, Final approval of the version to be published.

Dr. Deepa George - Concept and design of the work, Data analysis and interpretation, Drafting of the article, Final approval of the version to be published

Dr. Neena Thomas - Data analysis and interpretation, Drafting of the article, Critical revision of the article, Final approval of the version to be published

Dr. Bhagyasree Gopinath - Data analysis and interpretation, Drafting of the article, Critical revision of the article, Final approval of the version to be published.

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