ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 10, 2024

Efficacy and Safety of Dexmedetomidine vs. Butorphanol in Enhancing Analgesia with Hyperbaric Bupivacaine: A Hemodynamic Perspective

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ABSTRACT

Background- Spinal anaesthesia has been a widely utilized technique for various surgical procedures since its introduction. Despite the effectiveness of local anaesthetics, managing postoperative pain remains a challenge due to their limited duration of action. This study aimed to evaluate the analgesic efficacy and safety of intrathecal dexmedetomidine compared to butorphanol as adjuvants to hyperbaric bupivacaine, focusing specifically on their effects on hemodynamic parameters in patients undergoing infra-umbilical surgeries.

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Methods- A randomized control trial was conducted at the SMBT Institute of Medical Sciences and Research Centre, involving 72 patients scheduled for elective and emergency infra-umbilical surgeries. Participants were randomly assigned to two groups: Group D received bupivacaine with dexmedetomidine, while Group B received bupivacaine with butorphanol. Preoperative assessments were performed, and sensory and motor blockades were evaluated. Vital signs were monitored throughout the procedure, and statistical analyses were conducted to compare outcomes between the groups.

Results- The mean age of participants was 39.93 years, with no significant differences in demographic variables between groups. The dexmedetomidine group demonstrated a significantly faster onset of sensory blockade (0.66 vs. 2.2 minutes) and longer duration of analgesia (6.21 vs. 3.14 hours) compared to the butorphanol group ($p<0.01$). Vital sign monitoring revealed that Group B exhibited higher mean heart rates and mean arterial pressures at various time points, with significant differences noted at 3 minutes ($p=0.032$), 5 minutes ($p=0.017$), 3 hours ($p=0.015$), and 4 hours ($p=0.000$), indicating better hemodynamic stability in the dexmedetomidine group.

Conclusion- The addition of dexmedetomidine to bupivacaine in spinal anaesthesia significantly enhances the onset and duration of analgesia for infra-umbilical surgeries, making it a valuable adjunct in clinical practice.

Key-words- Bupivacaine, Dexmedetomidine, Infra-umbilical surgeries, Postoperative pain, Spinal anaesthesia

INTRODUCTION

Spinal anaesthesia, first introduced into clinical practice by August Bier in 1898 [1], has remained a widely utilized technique for both elective and emergency surgical procedures over the past century. Its enduring popularity is particularly evident in applications such as caesarean sections, lower abdominal surgeries, as well as orthopaedic and urological surgeries, among others [1,2].

Spinal anaesthesia is a widely utilized technique for lower abdominal and lower limb surgeries due to its cost-effectiveness and ease of administration. Common local anaesthetics employed in this procedure include lignocaine, bupivacaine, levobupivacaine, and ropivacaine. However, a significant challenge arises in postoperative pain management, as spinal anaesthesia with these local anaesthetics typically results in a relatively short duration

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of action. Consequently, early analgesic intervention is often necessary in the postoperative period to effectively manage pain [3].

Dexmedetomidine is a novel addition to the class of alpha-2 agonists, demonstrating numerous beneficial effects when administered via the epidural route [4]. This medication exerts its action on both pre- and post-synaptic sympathetic nerve terminals and the central nervous system, leading to a reduction in sympathetic outflow and a decrease in norepinephrine release. As a result, dexmedetomidine provides sedative, anti-anxiety, analgesic, sympatholytic, and hemodynamic effects [5-7]. While it can induce manageable hypotension and bradycardia, one of its most notable advantages is the absence of opioid-related side effects such as respiratory depression, pruritus, nausea, and vomiting [8-9].

Recent studies have indicated that alpha 2 adrenoceptor agonists can serve as effective adjuvants to spinal anaesthesia, demonstrating promising results in prolonging the duration of anaesthesia when administered both orally as a premedication and intravenously [10,11]. Additionally, butorphanol, characterized as a weak μ-receptor agonist and antagonist, is a lipid-soluble narcotic exhibiting strong k-receptor agonism. This combination of medications highlights the potential for enhanced efficacy in spinal anaesthetic practices [12-14]. In this study, we aimed to compare the analgesic efficacy and safety, specifically in terms of hemodynamic parameters, of intrathecal Dexmedetomidine versus Butorphanol when used as adjuvants to hyperbaric Bupivacaine in patients undergoing infraumbilical surgeries.

MATERIALS AND METHODS

This study was a randomized control trial conducted in the Department of Anaesthesiology at SMBT Institute of Medical Sciences and Research Centre in Igatpuri, Nashik, for two years. The study focused on patients scheduled for infra-umbilical surgeries within a tertiary care hospital setting. The sample size was determined using the formula $n= (Z\alpha/2 + Z\beta)2 \times (SD2) / d2$. Here, $Z\alpha/2$ represents the Z-value at a 5% error (1.96), $Z\beta$ is another Z-value at 20% (0.84), SD denotes the average standard deviation of the character and d refers to the mean difference. The mean and standard deviation for Butorphanol were 171.17 ± 23.99 minutes, while for Dexmedetomidine, they were 524.76 ± 375.43 minutes. Ultimately, the calculated sample size came out to be approximately n=36.

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Inclusion criteria- The study included ASA I and ASA II patients aged between 18 and 65 years who were posted for elective and emergency infra-umbilical surgeries with an anticipated duration of more than two hours.

Exclusion criteria- In this study, patients with neurological diseases, spinal deformities, and mental disorders and those suffering from local skin infections or diseases were excluded. Individuals with a history of anaphylaxis to local anesthetics, Dexmedetomidine, Butorphanol, or opioid dependence were also not considered. Patients who presented with abnormal electrocardiograms and those with coagulative or bleeding disorders were excluded as well. Additionally, pregnant patients scheduled for both obstetric and non-obstetric surgeries were not included in the study.

Methodology- Preoperative assessments were performed one day prior for elective cases and in the preoperative room for emergencies. Patients were randomly assigned to two groups: Group D received Bupivacaine with Dexmedetomidine, while Group B received Bupivacaine with Butorphanol. Both groups were preloaded with 10 ml/kg of Ringer lactate solution, and spinal anesthesia was administered using a 25G Quincke's needle in the L3-L4/L2-L3 space. Sensory blockade was assessed at 2-minute intervals for the first 20 minutes and then every 5 minutes until no further changes were observed. The onset and duration of sensory blockade were recorded, along with the need for rescue analgesia. The duration of motor blockade was recorded from the time of injection until the patient regained the ability to lift the extended leg. During the surgery, vital signs including heart rate, systolic and diastolic blood pressure, mean arterial pressure, and oxygen saturation (SpO_2) were monitored every 5 minutes for the first 30 minutes and then every 15 minutes until the end of the procedure. Patients were monitored for hypotension, bradycardia, nausea, vomiting, respiratory depression, and hypothermia. Specific interventions included IV fluids and Mephentermine for hypotension, Atropine for bradycardia, Ondansetron for nausea, oxygen for respiratory issues, and forced air warmers for hypothermia. Rescue analgesia was provided based on the Numerical Rating Scale (NRS) score.

Statistical analysis- Data was meticulously recorded in the study using a pre-designed study proforma. Qualitative data were analyzed and represented as frequency and percentage. In

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contrast, the association between qualitative variables was evaluated using the Chi-Square test with Continuity Correction for all 2 X 2 tables, alongside Fisher's exact test for cases involving 2 X 2 tables. Quantitative data were summarized using Mean ± SD. The quantitative data analysis between the two groups was conducted using an unpaired t-test when the data met the criteria of normality, and the Mann-Whitney Test was employed when the normality assumption was violated. A p-value of less than 0.05 was established as the threshold for statistical significance. Results were graphically illustrated where appropriate, utilizing SPSS Version 21.0 for most analyses and Microsoft Excel 2010 for graphical representation.

Ethical approval- The study was approved by the Institutional Review Board (IRB) of the SMBT Institute of Medical Sciences and Research Centre, Igatpuri, Nashik. Informed consent was obtained from all participants, ensuring their understanding of the study's purpose, procedures, and right to withdraw without affecting their medical care.

RESULTS

In the present study, 72 subjects undergoing infra-umbilical surgeries with spinal anesthesia (SA) were randomly assigned to one of two groups, each of 36 participants. The first group, designated as Group D, received a combination of Bupivacaine and Dexmedetomidine, while the second group, referred to as Group B, was administered Bupivacaine in conjunction with Butorphanol. This randomization was achieved using computer-generated random numbers to ensure unbiased allocation.

The mean age of the study cases was 39.93 years, with no difference between the study groups (p-0.65). Out of the total 70 cases, 79.2% were males and 20.8% were females with no difference between study groups (p=0.218). A total of 29.2% of cases were in ASA grade I, while 70.8% of cases were in ASA grade II. No difference was observed between the groups (p=0.19). The mean duration of surgery in groups B and D was 3.21 hours and 3.34 hours respectively (p=0.65).

The mean time of onset and achieving complete sensory block was significantly faster in dexmedetomidine group as compared to butorphanol (0.66 vs. 2.2 mins and 3.9 vs. 9.37 mins; $p<0.01$). Total duration and time to complete regression were also significantly more in cases of dexmedetomidine (6.21 vs 3.14 hrs and 6.32 vs. 3.31 hrs; $p<0.01$) (Fig. 1). However, the

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mean time of onset and to achieve complete motor block was significantly faster in dexmedetomidine group as compared to butorphanol (0.77 vs. 2.43 mins and 4.86 vs 10.23 mins; p<0.01). Total duration and time to complete regression were also significantly more in cases of dexmedetomidine (6.01 vs. 2.96 hrs and 6.05 vs 3.14 hrs; p<0.01) (Fig. 2).

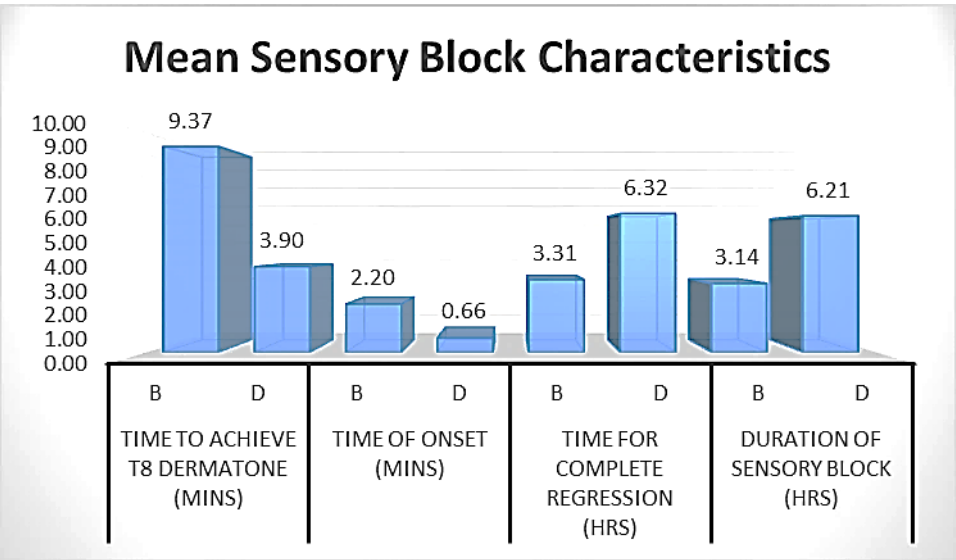

Fig. 1: Mean comparison of sensory block characteristics among study groups.

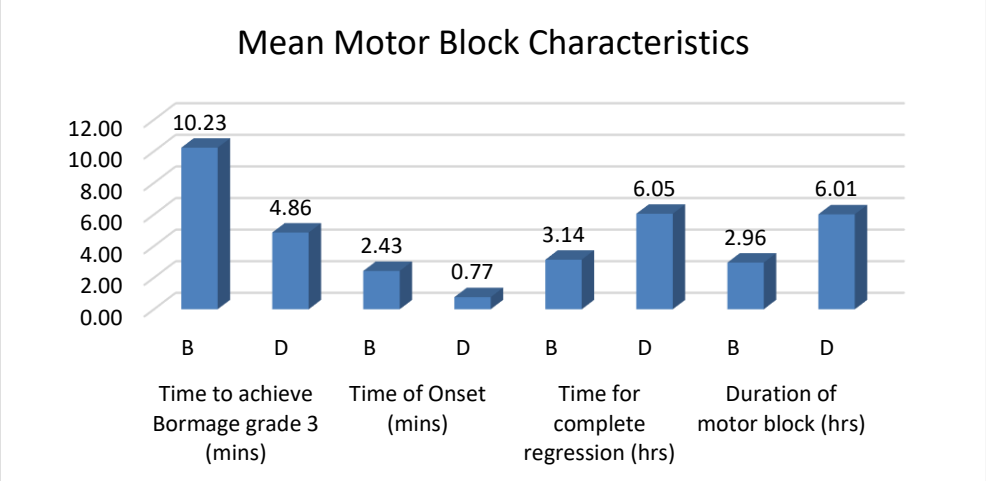

Fig. 2: Mean comparison of motor block characteristics among study groups.

The total duration of analgesia, as measured by mean time for the rescue analgesic requirement, was significantly longer in cases of the dexmedetomidine group (7.58 vs 4.49 hours; p<0.01). Fig. 3 compares mean heart rates between two groups (B and D) at various time intervals ranging from 1 minute to 24 hours. Overall, group B consistently exhibited

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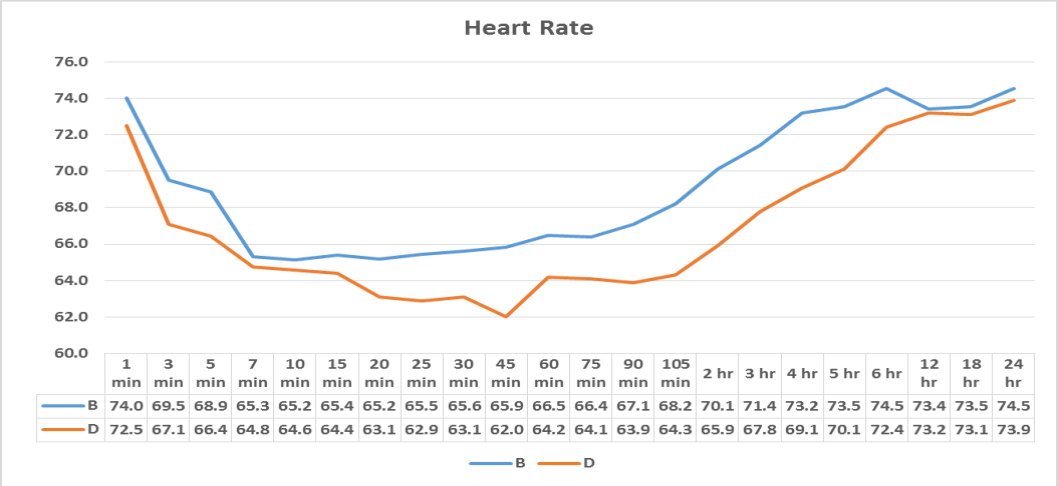
higher mean heart rates than group D across all time points, with statistically significant differences observed particularly at later intervals such as 90 minutes, 105 minutes, 2 hours, 3 hours, 4 hours, and beyond ($p<0.01$). The standard deviations suggest some variability within the groups; however, the p-values indicate that the differences in heart rates between the two groups are not statistically significant at earlier time points but become significant as time progresses.



	1 min	3 min	5 min	7 min	10 min	15 min	20 min	25 min	30 min	45 min	60 min	75 min	90 min	105 min	2 hr	3 hr	4 hr	5 hr	6 hr	12 hr	18 hr	24 hr
B	74.0	69.5	68.9	65.3	65.2	65.4	65.2	65.5	65.6	65.9	66.5	66.4	67.1	68.2	70.1	71.4	73.2	73.5	74.5	73.4	73.5	74.5
D	72.5	67.1	66.4	64.8	64.6	64.4	63.1	62.9	63.1	62.0	64.2	64.1	63.9	64.3	65.9	67.8	69.1	70.1	72.4	73.2	73.1	73.9

Fig. 3: Mean heart rate comparison among study groups.

Fig. 4 shows the mean arterial pressure (MAP) measured in mm Hg across different time intervals for two groups. Group B consistently shows higher MAP values than Group D at all time points, with statistically significant differences observed particularly at 45 minutes and beyond ($p < 0.01$). The MAP for Group B ranges from 100.1 mm Hg at 1 minute to 99.7 mm Hg at 6 hours, while Group D's MAP starts at 104.5 mm Hg and decreases to around 95.3 mm Hg by the end of the observation period. The p-values indicate that as time progresses, the difference in MAP between the two groups becomes increasingly significant.

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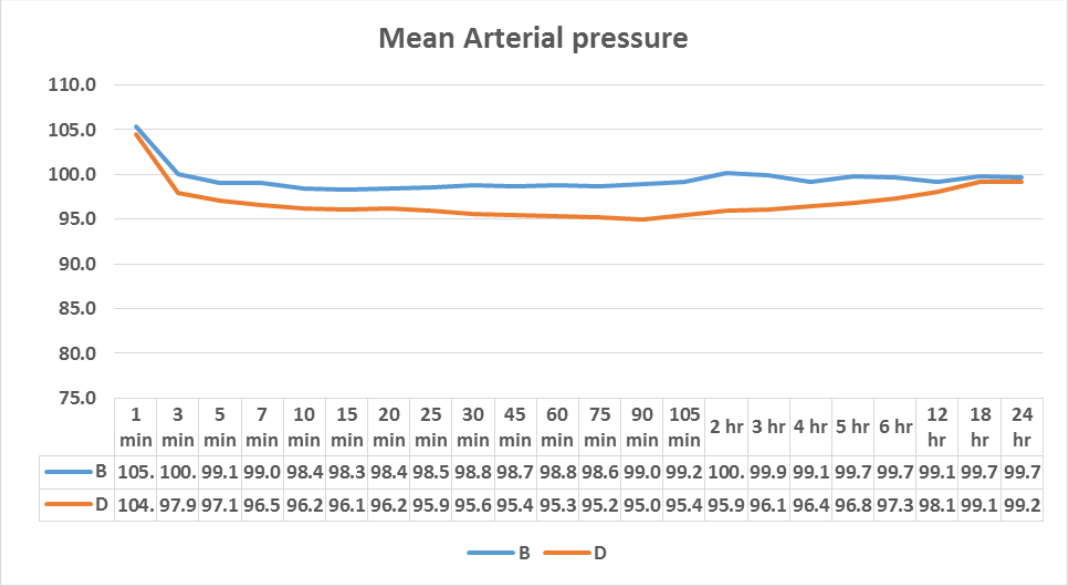

Fig. 4: Mean arterial pressure comparison among study groups.

Mean oxygen saturation comparison among study groups are represented in Fig. 5. Group B consistently shows higher SpO2 percentages compared to Group D across most time points, with statistically significant differences observed at 3 minutes (p=0.032), 5 minutes (p=0.017), 3 hours (p=0.015), and notably at 4 hours (p=0.000). The p-values indicate that the differences in SpO2 levels between the two groups are statistically significant at these specific time points. In contrast, other time intervals show no significant differences, suggesting that Group D's SpO2 levels may stabilize or improve over longer durations.

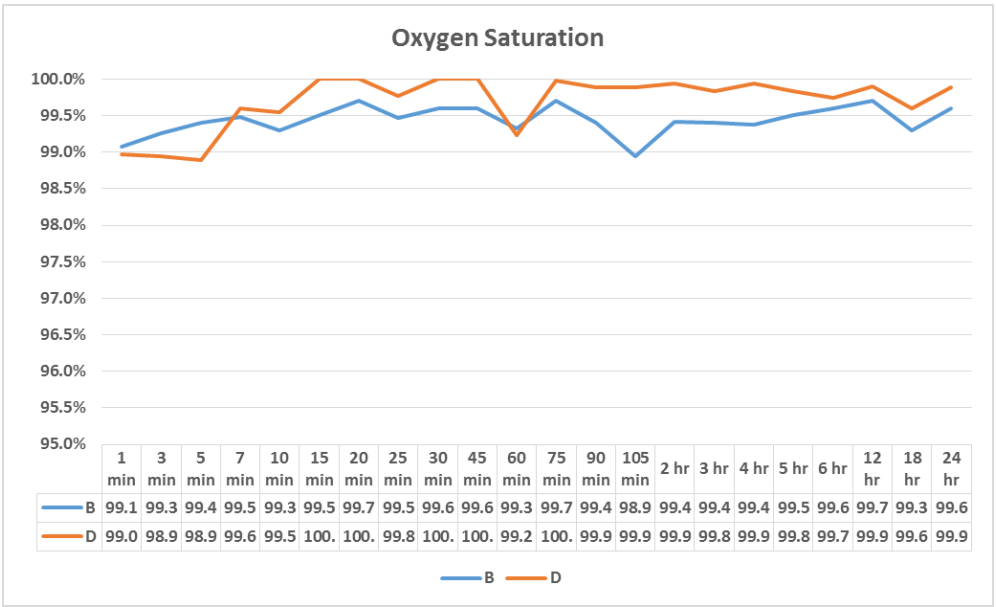

Fig. 5: Mean oxygen saturation comparison among study groups.

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The comparison of adverse reactions among the study groups reveals that none of the cases in any group experienced any episode of post-operative nausea and vomiting. However, 4 and 3 cases of dexmedetomidine group (11.4% and 8.3%) experienced hypotension and bradycardia during the surgery as compared to none in the butorphanol group (p=0.114; p=0.24) (Table 1).

Table 1: The comparison of adverse reactions among the study groups.

Complications	Group		Total	p-value
	B	D		
Hypotension	0	4	4	0.114
	0.0%	11.1%	5.6%	
Bradycardia	0	3	3	0.24
	0.0%	8.3%	4.2%	
PONV	0	0	0	NA
	0.0%	0.0%	0.0%	

DISCUSSION

Spinal anaesthesia is widely recognized as the preferred method for conducting lower abdominal and lower limb surgeries due to its cost-effectiveness and straightforward administration process. The local anaesthetic bupivacaine is predominantly utilized in this technique. However, a significant challenge arises in managing postoperative pain, as spinal anaesthesia that relies solely on local anaesthetics tends to have a limited duration of effectiveness. Consequently, this necessitates timely analgesic interventions following surgery to ensure adequate pain relief [3].

Dexmedetomidine is a highly selective α2-adrenoceptor agonist that has gained prominence in anesthesia. It is often used in combination with levobupivacaine for spinal anesthesia, where it has been shown to facilitate a shorter onset time and prolong both sensory and motor block. This combination not only enhances the effectiveness of the anesthesia but also contributes to improved hemodynamic stability, making it a favorable option for patients [4]. Additionally, dexmedetomidine is utilized for premedication and general anesthesia, demonstrating its versatility and efficacy in various anesthetic protocols [15-17]. Butorphanol is a lipid-soluble narcotic that acts as a weak agonist and antagonist at the μ-opioid receptors

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while exhibiting strong agonistic effects on the k-opioid receptors. When administered epidurally, butorphanol produces a dose-dependent increase in the duration of analgesia, effectively providing relief from postoperative pain [18].

In our study, measuring the total duration of analgesia, the meantime for the requirement of rescue analgesics was significantly longer in the dexmedetomidine group, with results showing 7.58 hours compared to 4.49 hours ($p<0.01$). Mahendru *et al*. observed that patients receiving dexmedetomidine experienced a significantly delayed need for rescue analgesics when compared to those receiving clonidine and fentanyl. Their findings concluded that intrathecal dexmedetomidine is associated with a reduced demand for rescue analgesics over 24 hours compared to clonidine, fentanyl, or bupivacaine alone [19]. Similarly, Chandra *et al*. [15] highlighted that dexmedetomidine is a potent and highly selective α2-adrenoreceptor agonist that provides both sedative and analgesic effects, asserting its superiority as an adjuvant over clonidine. Furthermore, Ganesh *et al*. confirmed that dexmedetomidine prolongs the duration of analgesia more effectively than clonidine [16].

Several studies have compared the efficacy of clonidine and butorphanol in providing postoperative analgesia. In a study conducted by Gupta *et al*. [20], it was found that clonidine offers a longer duration of both sensory and motor blockade, as well as extended postoperative analgesia when compared to butorphanol. Specifically, the need for rescue analgesia occurred significantly earlier in the butorphanol group (Group B), with an average time of 211.09 ± 20.74 minutes, compared to the clonidine group (Group C), which had an average time of 256.32 ± 24.40 minutes before requiring additional analgesics. Similarly, Shah *et al.* reported that the mean time to first request for analgesia was 278.7 ± 29.6 minutes in the clonidine group versus 218.6 ± 21.9 minutes in the butorphanol group, further supporting the findings of prolonged analgesic effects with clonidine [21]. Additionally, Ruku and Kassana observed that the duration of analgesia was significantly greater in the clonidine group (384.8 ± 12.42 minutes) compared to the butorphanol group (313.93 ± 9.23 minutes) [22]. These studies collectively indicate that clonidine may be more effective than butorphanol for postoperative pain management.

In a comparative analysis of hemodynamic parameters during surgery, both groups exhibited similar baseline mean heart rate and mean arterial pressure (MAP). However, the dexmedetomidine group demonstrated consistently lower heart rate and MAP throughout the surgical duration, with statistically significant differences observed from one hour to six

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hours post-administration ($p<0.05$). Chaudhary *et al.* [23] noted that while hemodynamic parameters did not show significant differences between the groups over the study period, values were still lower in the dexmedetomidine group. Similarly, Bharti *et al.* reported enhanced hemodynamic control with dexmedetomidine [24]. In contrast, Thomas *et al.* found that mean heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and MAP were comparable at baseline, following drug administration, and after induction between the two groups [25].

CONCLUSION

The present findings indicated that Dexmedetomidine outperformed Butorphanol in prolonging both the duration of motor and sensory block and delaying the time to the first analgesic request, thereby providing superior postoperative analgesia. However, some cases involving Dexmedetomidine experienced hypotension during surgery, although this difference was not statistically significant. In contrast, Butorphanol exhibited a slower onset and faster regression of effects, with fewer hypotension and bradycardia than Dexmedetomidine. Therefore, Butorphanol may be an effective alternative to Dexmedetomidine in surgical procedures where a quicker recovery is desired. Future research could explore the long-term effects of Butorphanol and Dexmedetomidine on patient recovery and pain management in various surgical settings.

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