# To Compare Effect of Intrathecal Dexmedetomidine versus Clonidine as an Adjuvant to 0.5% Hyperbaric Bupivacaine in Orthopaedic Lower Limb Surgeries under Spinal Anaesthesia - A Prospective Double Blind Randomised Control Study

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Abstract: <u>Background</u>: The aim of this study was to compare the effects of dexmedetomidine and clonidine used as adjuvants to 0.5 % hyperbaric bupivacaine in lower limb orthopaedic surgeries under spinal anaesthesia. <u>Material and Methods</u>: The prospective clinical study – Randomized controlled trail was conducted in ninety patients of any gender divided in three groups. In Group - C, Group - D, Group - N (n=30 each) patients received 50mcg of Clonidine (0.5ml), 5mcg of dexmedetomidine and 0.5ml normal saline along with 12.5mg of hyperbaric bupivacaine respectively for spinal anaesthesia. These groups were compared using one - way analysis of variance (ONE - WAY ANOVA) and difference between the groups compared using unpaired T - test. <u>Results</u>: Duration of analgesia was more with intrathecal dexmedetomidine. <u>Conclusion</u>: We concluded that the supplementation of bupivacaine with longer duration of sensory and motor block when compared to bupivacaine alone. Amongst dexmedetomidine and clonidine, dexmedetomidine shows significantly longer duration of analgesia than clonidine which proves it to be better adjuvant than clonidine at the mentioned dose

Keywords: Clonidine, Dexmedetomidine, Bupivacaine

## 1. Introduction

Bupivacaine is three to four times more potent than lignocaine<sup>1</sup>and has longer duration of action. Its disadvantages are slow onset of action and decreased motor block. Hyperbaric bupivacaine 0.5% is extensively used in India for spinal anaesthesia. Though the duration of action of bupivacaine is prolonged, it does not produce prolonged post – operative analgesia. Hence, an adjuvant is required for producing prolonged post - operative analgesia. The discovery of opioid receptors and endorphins in spinal and supra - spinal regions soon led to the use of spinal opiates. Morphine was the first opioid administered intrathecally to augment neuraxial blocks.2

Recently  $\alpha$  - 2 adrenoreceptor agonists have been used as adjuvants to local anaesthetic agents because of their sedative, analgesic and haemo dynamic stabilizing effect. They have been found to prolong the duration of spinal block following intrathecal administration.3

Clonidine, an  $\alpha$  - 2 adrenergic agonist, has a variety of different actions. Oral clonidine was used to prolong spinal anaesthesia. Hypotension was more pronounced after oral than intrathe calclonidine. 4 Addition of intra the calclonidine to bupivacaine prolongs analgesia and decreases morphine consumption postoperatively more than oral clonidine. Clonidine has antihypertensive properties and the ability to potentiate the effects of local /anaesthetics.5

Clonidine has been shown to result in prolongation of the sensory blockade and reduction in the volume or concentration of local anesthetic required to produce post – operative analgesia. Clonidine also has the ability to prolong the motor blockade produced by bupivacaine. Large dose sofintra the calclonidine (as much as  $450\mu g$ ) without local anaesthetics provide sedation and intense and long lasting postoperative analgesia, are inadequate for surgical anaesthesia and for this reason, clonidine has been used as anadjuvant to local anaesthetics rather than used alone.6

Dexmedetomidine also an  $\alpha$  - 2 adrenergic agonist is pharmacologically related to clonidine and is the most recent

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agent in this group approved by FDA in 1999 for the use in humans as short term medication (<24 hrs) for analgesia and sedation in intensive care unit. Its unique properties render it suitable for sedation and analgesia during the whole of perioperative period. Various studies have also found that intravenous dexmedetomidinecan decrease the haemodynamic response to laryngoscopy and intubation.

# 2. Methods

The prospective clinical study – Randomized controlled trail was conducted under the Department of Anaesthesiology, Jhalawar medical college and hospital, Jhalawar, Rajasthan. After getting IEC permission, all the patients were evaluated thoroughly before the anaesthesia by taking H/O present and past illness. Vital parameters were checked, and General physical and systemic and local examination were done to make fitness. All the possible following investigation were done as required.

#### **Inclusion Criteria:**

- ASA 1 & II
- AGE 18 60 years, of either sex
- Orthopaedic procedures of Lower Limbs.
- Weight 50 80 kg.
- Height > 150 cm.

#### **Exclusion Criteria:**

- ASA III & IV
- Bleeding diathesis
- Pregnancy
- Spinal Deformity
- Age 65 years
- CNS disorder
- Local anaesthetic sensitivity
- Local Sepsis

#### Pre - operative preparation:

All the patients were explained about the procedure and informed consent were obtained. Tablet diazepam 10 mg was given as preoperative night sedation. Patients were made familiar with the visual analogue scale (VAS) and were trained to use it adequately. Bupivacaine sensitivity was tested. Informed consent was obtained. Pre - operative fasting for 6 hrs for solids, 4 hrs for clear liquids. Vital signs were recorded on the day of surgery. No premedication was given to any patient on morning of surgery.

#### Anaesthetic procedure:

#### Sub arachnoid block: -

On arrival at operation theatre, basic monitoring was established with ECG, NIBP and pulse oximeter. Intravenous line was started with 18G iv canula on the left forearm and preloaded with a crystalloid (RL) 10ml/kg, prior to sub - arachnoid block to all patients.

Spinal anaesthesia was performed at L3 - L4 interspace with the patient in left lateral position by using a 25 Gauge Quincke needle under strict aseptic conditions. Free flow of cerebrospinal fluid was verified before injection of the anaesthetic solution 3.0 ml volume, which was administered over 30 seconds. The direction of the needle aperture was kept cranially during the injection. All patients were immediately placed in a supine position. Monitoring was done using continuous electrocardiography, heart rate, non invasive blood pressure and continuous pulse oximetry and patients were given 6.0 L/min of oxygen by Hudson's face mask.

Vitals were checked every 5 minutes for first 30 minutes then every 10 minutes till surgery and then every 30 minutes for 6 hours postoperatively. When adequate spinal block was achieved, the time from the end of intrathecal injection to readiness for surgery was recorded. Then the patient was positioned for planned surgery. Patients were monitored and different time intervals were noted to calculate the onset and duration of sensory and motor blockade. After completion of surgery patients were shifted to post - operative ward and duration of analgesia were noted. The following observations were taken:

## 3. Results

Age (years)	Group C (n=30)	Group D (n=30)	Group N (n=30)	P value
Mean $\pm$ SD	46.9 ± 11.65	42.13 ± 10.97	45.33 ± 10.2	C vs D: 0.096 C vs N: 0.581 D vs N: 0.261
Male: female	7: 23	6: 24	8: 22	C vs D: 0.754 <sup>†</sup> C vs N: 0.766 <sup>†</sup> D vs N: 0.542 <sup>†</sup>
ASA (I: II)	17: 13	20: 10	19: 11	C vs D: 0.426 <sup>†</sup> C vs N: 0.598 <sup>†</sup> D vs N: 0.787 <sup>†</sup>

**Table 1:** Comparison of age (years) between group C, D and N.

**Table 2:** Comparison of onset and duration time between group C, D and N.

Onset and duration time	Group C ( $n=30$ )	Group $D$ (n=30)	Group N ( $n=30$ )	P value
Sensory block onset time (minutes)				
1	15 (50%)	24 (80%)	0 (0%)	<.0001*
2	15 (50%)	6 (20%)	13 (43.33%)	C vs D: 0.015 <sup>†</sup>
3	0 (0%)	0 (0%)	14 (46.67%)	C vs N: <.0001*
4	0 (0%)	0 (0%)	3 (10%)	D vs N: <.0001*

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Motor block onset time (minutes)						
1	9 (30%)	22 (73.33%)	0 (0%)	.0001*		
2	21 (70%)	8 (26.67%)	0 (0%)	<.0001		
3	0 (0%)	0 (0%)	10 (33.33%)	$C vs D: 0.0008^{\circ}$		
4	0 (0%)	0 (0%)	12 (40%)	$D_{VS} N < 0001^*$		
5	0 (0%)	0 (0%)	8 (26.67%)	D VS IV. <.0001		
Duration of motor blockade (minutes)	280.77 ± 24.22	303.33 ± 33.73	$164.27 \pm 24.05$	<.0001 <sup>‡</sup> C vs D: 0.002 C vs N: <.0001 D vs N: <.0001		
Duration of analgesia (minutes)	343.27 ± 24.64	366.13 ± 36.55	190.13 ± 27.44	<.0001 <sup>‡</sup> C vs D: 0.004 C vs N: <.0001 D vs N: <.0001		
Duration of sensory blockade (minutes)	365.37 ± 23.59	398.53 ± 31.33	$205.1 \pm 30.36$	<.0001 <sup>‡</sup> C vs D: <.0001 C vs N: <.0001 D vs N: <.0001		

\* Fisher's exact test, <sup>†</sup> Chi square test, <sup>‡</sup> ANOVA

Proportion of patients with sensory block onset time (minutes): - 2 was significantly higher in group C and group N as compared to group D. (2: - 50%, 43.33% vs 20% respectively). Proportion of patients with sensory block onset time (minutes): - 1 was significantly higher in group D as compared to group C (p value=0.015) and group N (p value<.0001). (1: - 80% vs 50%, 0% respectively). Proportion of patients with sensory block onset time (minutes): - 3, 4 was significantly higher in group N as compared to group C (p value<.0001) and group N (p value<.0001). (3: - 46.67% vs 0%, 0% respectively, 4: - 10% vs 0%, 0% respectively).

Proportion of patients with motor block onset time (minutes): - 2 was significantly higher in group C as compared to group D and group N. (2: - 70% vs 26.67%, 0% respectively). Proportion of patients with motor block onset time (minutes): - 1 was significantly higher in group D as compared to group C (p value=0.0008) and group N (p value<.0001). (1: - 73.33% vs 30%, 0% respectively). Proportion of patients with motor block onset time (minutes): - 3, 4, 5 was significantly higher in group N as compared to group C (p value<.0001) and group N as compared to group C (p value<.0001) and group N as compared to group C (p value<.0001) and group D (p value<.0001). (3: - 33.33% vs 0%, 0% respectively, 4: - 40% vs 0%, 0% respectively, 5: - 26.67% vs 0%, 0% respectively).

Significant difference was seen in duration of motor blockade (minutes), duration of analgesia (minutes), duration of sensory blockade (minutes) between group C, D and N. (p value <.05)

Mean  $\pm$  SD of duration of motor blockade (minutes) in group D was 303.33  $\pm$  33.73 which was significantly higher as compared to group C (280.77  $\pm$  24.22, p value=0.002) and group N (164.27  $\pm$  24.05, p value<.0001). Mean  $\pm$  SD of duration of motor blockade (minutes) in group C was significantly higher as compared to group N. (p value<.0001).

Mean  $\pm$  SD of duration of analgesia (minutes) in group D was 366.13  $\pm$  36.55 which was significantly higher as compared to group C (343.27  $\pm$  24.64, p value=0.004) and group N (190.13  $\pm$  27.44, p value<.0001). Mean  $\pm$  SD of duration of analgesia (minutes) in group C was significantly higher as compared to group N. (p value<.0001)

Mean  $\pm$  SD of duration of sensory blockade (minutes) in group D was 398.53  $\pm$  31.33 which was significantly higher as compared to group C (365.37  $\pm$  23.59, p value<.0001) and group N (205.1  $\pm$  30.36, p value<.0001). Mean  $\pm$  SD of duration of sensory blockade (minutes) in group C was significantly higher as compared to group N. (p value<.0001)

Post operative VAS score	Group C ( $n=30$ )	Group $D$ (n=30)	Group N $(n=30)$	P value
At 0 minute				
No pain	30 (100%)	30 (100%)	30 (100%)	NA
Mean ± SD	$0\pm 0$	$0\pm 0$	$0\pm 0$	1 <sup>‡</sup> C vs D: 1 C vs N: 1 D vs N: 1
At 2 minutes				
No pain	30 (100%)	30 (100%)	30 (100%)	NA
Mean ± SD	$0\pm 0$	$0\pm 0$	0 ± 0	1 <sup>‡</sup> C vs D: 1 C vs N: 1 D vs N: 1
At 5 minutes				
No pain	30 (100%)	30 (100%)	30 (100%)	NA
Mean ± SD	$0\pm 0$	$0\pm 0$	$0\pm 0$	$1^{\ddagger}$ C vs D: 1

 Table 3: Comparison of post operative VAS score between group C, D and N.

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At 10 minutes         Description         Description           No pain         30 (100%)         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: 1           At 20 minutes         No pain         30 (100%)         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: 1         C vs D: 1           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: 1         C vs D: 1           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: 1         D vs N: 1           At 45 minutes					C vs N: 1
No pain         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs N: 1           At 20 minutes         No pain         30 (100%)         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: 1         D vs N: 1           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: 1         C vs D: 1           No pain         30 (100%)         30 (100%)         30 (100%)         NA         1           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: 1         C vs N: 1           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs N: 1         D vs N: 1           At 45 minutes $C$ vs N: 1         D vs N: 1         D vs N: 1         D vs N: 1           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs N: 1         D vs N: 1           Moderate pain         0 (0%)         30 (100%)         2 (6.67%)         C vs N: N: NOI           Moderate pain         0 (0%)         0 (0%)         2 (6.67%)         C vs N: N	At 10 minutes				D VS N. 1
Mean $\pm$ SD $0 \pm 0$ $C$ vs D: 1 C vs N: 1           At 20 minutes         No pain         30 (100%)         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $C$ vs D: 1 C vs N: 1           At 30 minutes         No pain         30 (100%)         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $C$ vs D: 1 C vs N: 1           At 45 minutes           No pain         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: 1 D vs N: 1           At 60 minutes                Mo pain         30 (100%)         30 (100%)         2 (6.67%)         C vs D: N A           Mid pain         0 (0%)         0 (0%)         2 (7.667%)         C vs D: N A           Moderate pain         0 (0%)         0 (0%)         1 (3.33%)         D vs N: <.0001           Mean $\pm$ SD <td>No pain</td> <td>30 (100%)</td> <td>30 (100%)</td> <td>30 (100%)</td> <td>NA</td>	No pain	30 (100%)	30 (100%)	30 (100%)	NA
At 20 minutes         No pain         30 (100%)         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $C$ vs N: 1           At 30 minutes $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ NA           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $V = N$ $V = N$ At 45 minutes $V = 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $NA$ At 45 minutes $V = 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $V = N$ $V = N$ At 60 minutes $V = 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: NA           Mid pain $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ $C$ vs N: $0 = N$ Moderate pain $0 (0\%)$ $0 (0\%)$ $2 (5.67\%)$ $C$ vs N: $0 = N$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $1 \pm 0$ $C$ vs N: $0 = N$ Moderate pain $0 (0\%)$ $0 (0\%)$ $1 (3 \cdot 3\%)$ $D$ vs N: $(0 \circ 0)^{2}$ Mid pain $0 (0\%)$ $0 (0\%)$	Mean ± SD	0 ± 0	0 ± 0	0 ± 0	1 <sup>‡</sup> C vs D: 1 C vs N: 1 D vs N: 1
No pain         30 (100%)         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $1^{+}$ $C vs D: 1$ $D vs N: 1$ At 30 minutes $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $D \pm N: 1$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $D vs N: 1$ At 45 minutes $V$	At 20 minutes				
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	No pain	30 (100%)	30 (100%)	30 (100%)	NA
At 30 minutes         30 (100%)         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: 1           At 45 minutes $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $D \times N$ : 1           At 45 minutes $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $D \times N$ : 1           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $D \pm 0$ $D \pm N$ : 1           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $D \times N$ : 1           At 60 minutes $0 \pm 0$ $0 (0\%)$ $2 (6.67\%)$ $C 0001^*$ $C \times N$ : 1           Moderate pain $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ $C \times N$ : 20001 $C \times N$ $C \times N$ : 20001           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $1 \pm 3 \pm 0.61$ $C \times N$ : $C \times 0001^*$ Moantes $0 \pm 0$ $0 \pm 0$ $0 (0\%)$ $5 (16.67\%)$ $C \times N$ : $C \times 001^*$ Mild pain $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $5 (16.67\%)$ $C \times N$ : $C \times$	Mean ± SD	0 ± 0	0 ± 0	0 ± 0	1 <sup>+</sup> C vs D: 1 C vs N: 1 D vs N: 1
No pain $30(100\%)$ $30(100\%)$ $30(100\%)$ $10\%$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $1^{\pm}$ C vs N: 1         D vs N: 1         D vs N: 1         D vs N: 1         D vs N: 1           At 45 minutes         0 $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: 1           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: NA           At 60 minutes         0 $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ $C$ vs D: NA           Moderate pain $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ $C$ vs N: $< 0001^{\dagger}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $1 (3.33\%)$ D vs N: $< 0001^{\dagger}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $1 (3.33\%)$ D vs N: $< 0001^{\dagger}$ Moderate pain $0 (0\%)$ $0 (0\%)$ $5 (16.67\%)$ $C$ vs D: NA           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $2 (8 3.33\%)$ D vs N: $< 0001^{\dagger}$ Moderate pain $0 (0\%)$ $0 (0\%)$ $2 (0 \sqrt{5} 3 \pm 1.53)$ $C$ vs D: NA	At 30 minutes	30 (100%)	30 (100%)	30 (100%)	NA
Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ VS         D: C         VS         D: C         VS         D: VS         <	NO pain	30 (10070)	30 (10070)	30 (100%)	1‡
At 45 minutes         No pain         30 (100%)         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs D: 1           At 60 minutes         No pain         30 (100%)         30 (100%)         2 (.667%)         <0001 <sup>3</sup> Mild pain         0 (0%)         0 (0%)         2 (.667%)         C vs D: NA           Moderate pain         0 (0%)         0 (0%)         1 (.3.33%)         D vs N: <.0001 <sup>3</sup> Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ 1.8 $\pm 0.61$ C vs D: 1         C vs N: <.0001 <sup>3</sup> Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ 1.8 $\pm 0.61$ C vs D: NA         C vs N: <.0001 <sup>4</sup> Mean $\pm$ SD $0 \pm 0$ $0 (0\%)$ 5 (16.67%)         C vs D: NA         C vs N: <.0001 <sup>*</sup> Moderate pain         0 (0%)         0 (0%)         25 (83.33%)         D vs N: <.0001 <sup>*</sup> Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $3 \pm 0.74$ C vs D: NA         C vs N: <.0001 <sup>*</sup> Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $3 \pm 0.74$ C vs N: <.0001 <sup>*</sup> C vs N: <.0001 <sup>*</sup> Mild pain         0 (0%)         0 (0%) </td <td>Mean ± SD</td> <td>0 ± 0</td> <td>0 ± 0</td> <td>0 ± 0</td> <td>C vs D: 1 C vs N: 1 D vs N: 1</td>	Mean ± SD	0 ± 0	0 ± 0	0 ± 0	C vs D: 1 C vs N: 1 D vs N: 1
No pain         30 (100%)         30 (100%)         NA           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $1^{\pm}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $C$ vs N: 1           No pain         30 (100%) $0 (0\%)$ $2 (6.67\%)$ $C 0001^{+}$ Mild pain $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ $C$ vs N: $< 0001^{-}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $1 (3.33\%)$ $D$ vs N: $< 0001^{+}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $1 (3.33\%)$ $D$ vs N: $< 0001^{+}$ Modarate pain $0 (0\%)$ $0 \pm 0$ $1 (3.33\%)$ $C$ vs N: $< 0001^{+}$ Mold pain $0 (0\%)$ $0 (0\%)$ $5 (16.67\%)$ $C$ vs N: $< 0001^{+}$ Modarate pain $0 (0\%)$ $0 (0\%)$ $2 (0 0.5^{+})$ $C$ vs N: $< 0001^{+}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $3 \pm 0.74$ $C$ vs N: $< 0001^{+}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $3 \pm 0.74$ $C$ vs N: $< 0001^{+}$ Mean $\pm$ SD $0 \pm 0$ $0 (0\%$	At 45 minutes	20 (100%)	20 (1000()	20 (100%)	NT A
Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $\begin{bmatrix} C & vs & D: & 1 \\ C & vs & N: & 1 \\ D & vs & N: & 1 \\ Mild pain         0 (0\%) 30 (100\%) 2 (6.67\%) < 0001^*           Mild pain         0 (0\%) 0 (0\%) 27 (90\%)         C vs & D: NA cvs N: < 0001^*           Moderate pain         0 (0\%) 0 (0\%) 1 (3.33\%) Dvs N: < 0001^*           Mean \pm SD         0 \pm 0 0 \pm 0 1.8 \pm 0.61         C vs D: NA           No pain         30 (100\%) 0 (0\%) 5 (16.67\%)         C vs N: < 0001^*           Mild pain         0 (0\%) 0 (0\%) 5 (16.67\%)         C vs N: < 0001^*           Moderate pain         0 (0\%) 0 (0\%) 5 (16.67\%)         C vs N: < 0001^*           Mean \pm SD         0 \pm 0 0 \pm 0 3 \pm 0.74         C vs N: < 0001^*           Mild pain         0 (0\%) 0 (0\%) 4 (13.33\%)         C vs N: < 0001^*           Moderate pain         0 (0\%) 0 (0\%) 4 (13.33\%)         C vs N: < 0001^*           Maan \pm SD         0 \pm 0 0 \pm 0 $	No pain	30 (100%)	30 (100%)	30 (100%)	NA 1 <sup>‡</sup>
At 60 minutes         No pain         30 (100%)         30 (100%)         2 (6.67%) $< 0001^*$ Mild pain         0 (0%)         0 (0%)         27 (90%)         C vs D: NA           Moderate pain         0 (0%)         0 (0%)         1 (3.33%)         D vs N: $< 0001^*$ Mean $\pm$ SD         0 $\pm$ 0         0 $\pm$ 0         1 (3.33%)         D vs N: $< 0001^*$ Mean $\pm$ SD         0 $\pm$ 0         0 $\pm$ 0         1.8 $\pm$ 0.61         C vs D: NA           Mid pain         0 (0%)         0 (0%)         0 (0%) $< 0001^+$ Mid pain         0 (0%)         0 (0%)         5 (16.67%)         C vs D: NA           Moderate pain         0 (0%)         0 (0%)         25 (83.33%)         D vs N: $< 0001^+$ Mean $\pm$ SD         0 $\pm$ 0         0 $\pm$ 0 $\pm$ 0 $\pm$ 0 $=$ 0 $\times$ 0 $\times$ N: $< 0001^+$ Mean $\pm$ SD         0 $\pm$ 0         0 $\pm$ 0 $\pm$ 0 $=$ 0 $\times$ N: $< 0001^+$ Mid pain         0 (0%)         30 (100%)         0 (0%)         C vs N: $< 0001^+$ Mean $\pm$ SD         0 $\pm$ 0         0 $\pm$ 0 $=$ 0 $\times$ N: $< 0001^+$ C vs N: $< 0001^+$ Mid pain         0 (0%)         0 (0%)         2 (66.67%)	Mean ± SD	0 ± 0	0 ± 0	0 ± 0	C vs D: 1 C vs N: 1 D vs N: 1
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	At 60 minutes				
Mild pain         0 (0%)         0 (0%)         27 (90%)         C vs D: NA C vs N: <0001*           Moderate pain         0 (0%)         0 (0%)         1 (3.33%)         D vs N: <0001*	No pain	30 (100%)	30 (100%)	2 (6.67%)	<.0001*
Moderate pain         0 (0%)         0 (0%)         1 (3.33%)         C vs N: <0001 D vs N: <0001           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $1.8 \pm 0.61$ C vs D: 1 C vs N: <0001	Mild pain	0 (0%)	0 (0%)	27 (90%)	C vs D: NA
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Moderate pain	0 (0%)	0 (0%)	1 (3.33%)	C vs N: $<.0001$ D vs N: $<.0001^*$
At 90 minutes         30 (100%)         30 (100%)         0 (0%) $<.0001^*$ Mild pain         0 (0%)         0 (0%)         5 (16.67%)         C vs D: NA           Moderate pain         0 (0%)         0 (0%)         25 (83.33%)         D vs N: $<.0001^*$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $2 \pm 0.74$ C vs D: NA $<.0001^{\ddagger}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $3 \pm 0.74$ C vs D: NA $C vs N: <.0001$ Mild pain         0 (0%)         30 (100%)         0 (0%) $C vs D: NA$ C vs D: NA           Moderate pain         0 (0%)         0 (0%)         4 (13.33%)         C vs D: NA         C vs N: <.0001^*	Mean ± SD	0 ± 0	0 ± 0	$1.8 \pm 0.61$	<.0001* C vs D: 1 C vs N: <.0001 D vs N: <.0001
No pair $30(100\%)$ $30(100\%)$ $50(10\%)$ $50(10\%)$ <td>At 90 minutes</td> <td>20 (100%)</td> <td>20 (100%)</td> <td>0 (0%)</td> <td>&lt; 0001*</td>	At 90 minutes	20 (100%)	20 (100%)	0 (0%)	< 0001*
Mild pain $0(0\%)$	No pain Mild pain	30(100%)	30(100%)	0(0%) 5(1667%)	<.0001
Moderate pain         0 (0%)         0 (0%)         25 (83.33%)         D vs N: <.0001*           Mean $\pm$ SD         0 $\pm$ 0         0 $\pm$ 0         0 $\pm$ 0         3 $\pm$ 0.74         C vs D: 1 C vs N: <.0001		0 (070)	0 (070)	5 (10.0770)	C vs D: 101 C vs N: <.0001*
Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $3 \pm 0.74$ $\stackrel{< .0001^{\ddagger}}{C}$ $C \text{ vs } \text{ D: } 1$ $C \text{ vs } \text{ N: } < .0001$ At 120 minutes $0 0 0 0 0$ $30 (100\%)$ $30 (100\%)$ $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $C \text{ vs } \text{ N: } < .0001^{\ast}$ Moderate pain $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $26 (86.67\%)$ $C \text{ vs } \text{ N: } < .0001^{\ast}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $26 (86.67\%)$ $C \text{ vs } \text{ N: } < .0001^{\ast}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $26 (86.67\%)$ $C \text{ vs } \text{ N: } < .0001^{\ast}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $2 (667\%)$ $C \text{ vs } \text{ N: } < .0001^{\ast}$ Moldrate pain $0 (0\%)$ $30 (100\%)$ $0 (0\%)$ $C \text{ vs } \text{ N: } < .0001^{\ast}$ Mean $\pm$ SD $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $C \text{ vs } \text{ N: } < .0001^{\ast}$ Mean $\pm$ SD $0 \pm 0$ $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $C \text{ vs } \text{ N: } < .0001^{\ast}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ <td>Moderate pain</td> <td>0 (0%)</td> <td>0 (0%)</td> <td>25 (83.33%)</td> <td>D vs N: &lt;.0001*</td>	Moderate pain	0 (0%)	0 (0%)	25 (83.33%)	D vs N: <.0001*
At 120 minutes           No pain         30 (100%)         30 (100%)         0 (0%) $< 0001^*$ Mild pain         0 (0%)         0 (0%)         4 (13.33%)         C vs D: NA           Moderate pain         0 (0%)         0 (0%)         26 (86.67%)         D vs N: <.0001*           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $25.3 \pm 1.53$ C vs D: 1         C vs N: <.0001           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $2 (6.67\%)$ C vs D: 1         C vs N: <.0001           Mtild pain         0 (0%)         0 (0%)         2 (6.67%)         C vs D: NA           Moderate pain         0 (0%)         0 (0%)         2 (6.67%)         C vs D: NA           Moderate pain         0 (0%)         0 (0%)         2 (6.67%)         C vs N: <.0001*           Mild pain         0 (0%)         0 (0%)         2 (70%)         D vs N: <.0001*           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ C vs N: <.0001*           Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ C vs N: <.0001*           Mean $\pm$ SD $0 \pm 0$ $13 (43.33\%)$ $0 (0\%)$ C vs N: <.0001*	Mean ± SD	0 ± 0	0 ± 0	3 ± 0.74	<.0001 <sup>‡</sup> C vs D: 1 C vs N: <.0001 D vs N: <.0001
No pain         30 (100%)         30 (100%)         0 (0%) $(0\%)$ $(0\%)$ $(0\%)$ $(13.33\%)$ $(0\%)$ $(13.33\%)$ $(0\%)$ $(10\%)$	At 120 minutes	20 (100%)	20 (1000()	0 (00)	
Mild pail $0 (0\%)$ $0 (0\%)$ $4 (13.53\%)$ $C vs D. NA$ Moderate pain $0 (0\%)$ $0 (0\%)$ $26 (86.67\%)$ $C vs N: <.0001^*$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $5.3 \pm 1.53$ $C vs D: 1$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $5.3 \pm 1.53$ $C vs D: 1$ No pain $30 (100\%)$ $30 (100\%)$ $0 (0\%)$ $2 (6.67\%)$ $C vs D: NA$ Moderate pain $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ $C vs D: NA$ Moderate pain $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ $C vs D: NA$ Moderate pain $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ $C vs D: NA$ Mean $\pm SD$ $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ $C vs D: NA$ Mean $\pm SD$ $0 (0\%)$ $0 (0\%)$ $2 (0.01^*$ $C vs D: N < .0001^*$ Mean $\pm SD$ $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ $C vs D: < 1001^*$ Moderate pain $0 (0\%)$ $13 (43.33\%)$ $0 (0\%)$ $C vs D: < .0001^*$ <th< td=""><td>No pain Mild noin</td><td>30 (100%)</td><td>30 (100%)</td><td>0(0%)</td><td>&lt;.0001 C vs D: NA</td></th<>	No pain Mild noin	30 (100%)	30 (100%)	0(0%)	<.0001 C vs D: NA
Moderate pain $0 (0\%)$ $0 (0\%)$ $26 (86.67\%)$ $D vs N: <.0001^*$ $D vs N: <.0001^*$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $5.3 \pm 1.53$ $C vs D: 1$ $C vs N: <.0001$ At 180 minutesNo pain $30 (100\%)$ $30 (100\%)$ $0 (0\%)$ $coon1^*$ Mild pain $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ $C vs D: NA$ Moderate pain $0 (0\%)$ $0 (0\%)$ $21 (70\%)$ $C vs N: <.0001^*$ Severe pain $0 (0\%)$ $0 (0\%)$ $7 (23.33\%)$ $D vs N: <.0001^*$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ $C vs D: 1$ $C vs N: <.0001$ At 4 hours $0 (0\%)$ $13 (43.33\%)$ $0 (0\%)$ $coon1^*$ No pain $0 (0\%)$ $17 (56.67\%)$ $0 (0\%)$ $C vs D: <.0001^*$ Mild pain $7 (23.33\%)$ $17 (56.67\%)$ $0 (0\%)$ $C vs D: <.0001^*$ Moderate pain $23 (76.67\%)$ $0 (0\%)$ $24 (80\%)$ $C vs N: <.0003^*$ Mucar LD $2 0 0 0 \%$ $0 0 0 0 0 0 \%$ $0 0 0 0 \%$ $0 0 0 0 \%$		0(0%)	0(0%)	4 (13.33%)	C vs D. NA $C vs N' < 0001^*$
Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $5.3 \pm 1.53$ $< 0001^{\ddagger}$ C vs D: 1 C vs N: <.0001 D vs N: <.0001At 180 minutesNo pain $30 (100\%)$ $30 (100\%)$ $0 (0\%)$ $< 0001^{\ddagger}$ C vs D: NA C vs N: <.0001^{\ddagger}Moderate pain $0 (0\%)$ $0 (0\%)$ $21 (70\%)$ C vs D: NA C vs N: <.0001^{\ddagger}Mean $\pm$ SD $0 \pm 0$ $0 (0\%)$ $7 (23.33\%)$ D vs N: <.0001^{\ddagger} C vs D: 1 C vs N: <.0001	Moderate pain	0 (0%)	0 (0%)	26 (86.67%)	D vs N: $<.0001^*$
At 180 minutes           No pain $30 (100\%)$ $30 (100\%)$ $0 (0\%)$ $<.0001^*$ Mild pain $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ C vs D: NA           Moderate pain $0 (0\%)$ $0 (0\%)$ $21 (70\%)$ C vs N: $<.0001^*$ Severe pain $0 (0\%)$ $0 (0\%)$ $7 (23.33\%)$ D vs N: $<.0001^*$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ $<0001^*$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ $<0001^*$ Mopain $0 (0\%)$ $13 (43.33\%)$ $0 (0\%)$ $<.0001^*$ Mild pain $7 (23.33\%)$ $17 (56.67\%)$ $0 (0\%)$ $<0001^*$ Moderate pain $23 (76.67\%)$ $0 (0\%)$ $24 (80\%)$ C vs N: $0.0003^*$ Severe pain $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $0 200 - 0.00$ $0 200 - 0.00$	Mean ± SD	0 ± 0	0 ± 0	5.3 ± 1.53	<.0001 <sup>‡</sup> C vs D: 1 C vs N: <.0001 D vs N: <.0001
No pain $30 (100\%)$ $30 (100\%)$ $0 (0\%)$ $<.0001^*$ Mild pain $0 (0\%)$ $0 (0\%)$ $2 (6.67\%)$ C vs D: NA           Moderate pain $0 (0\%)$ $0 (0\%)$ $21 (70\%)$ C vs N: $<.0001^*$ Severe pain $0 (0\%)$ $0 (0\%)$ $7 (23.33\%)$ D vs N: $<.0001^*$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ $C$ vs D: 1         C vs N: $<.0001$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ C vs N: $<.0001$ Mathematical Signature $0 \pm 0$ $13 (43.33\%)$ $0 (0\%)$ $<.0001^*$ Mild pain $7 (23.33\%)$ $17 (56.67\%)$ $0 (0\%)$ C vs D: $<.0001^*$ Moderate pain $23 (76.67\%)$ $0 (0\%)$ $24 (80\%)$ C vs N: $0.0003^*$ Severe pain $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $0 x N : <.0001^*$	At 180 minutes				*
Mind pain $0 (0\%)$ $0 (0\%)$ $2 (6.0\%)$ $C vs D: NA$ Moderate pain $0 (0\%)$ $0 (0\%)$ $21 (70\%)$ $C vs N: <.0001^*$ Severe pain $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $7 (23.33\%)$ $D vs N: <.0001^*$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ $c vs D: 1$ $c vs N: <.0001$ Mean $\pm$ SD $0 \pm 0$ $13 (43.33\%)$ $0 (0\%)$ $c.0001^*$ $c vs N: <.0001$ Mild pain $7 (23.33\%)$ $17 (56.67\%)$ $0 (0\%)$ $c vs D: -0.001^*$ Moderate pain $23 (76.67\%)$ $0 (0\%)$ $24 (80\%)$ $C vs N: 0.0003^*$ Severe pain $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $0 c 0.00^*$ $0 c 0.00^*$	No pain Mild pain	30 (100%)	30 (100%)	0(0%)	<.0001 C
Modelate pair $0(0\%)$ $0(0\%)$ $21(0\%)$ $C vs N. <.0001^*$ Severe pain $0(0\%)$ $0(0\%)$ $7(23.33\%)$ $D vs N: <.0001^*$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ $C vs D: 1$ $C vs N: <.0001$ $C vs N: <.0001$ $C vs N: <.0001$ At 4 hours $0(0\%)$ $13(43.33\%)$ $0(0\%)$ $<.0001^*$ Mild pain $7(23.33\%)$ $17(56.67\%)$ $0(0\%)$ $C vs N: <.0001^*$ Moderate pain $23(76.67\%)$ $0(0\%)$ $24(80\%)$ $C vs N: 0.0003^*$ Severe pain $0(0\%)$ $0(0\%)$ $0(0\%)$ $0 vs N: <.0001^*$	Milid pain Moderate pain	0(0%)	0(0%)	2(0.07%) 21(70%)	C vs D: NA $C vs N < 0001^*$
Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ $<0001^{\ddagger}$ Mean $\pm$ SD $0 \pm 0$ $0 \pm 0$ $5.8 \pm 1.32$ $<0001^{\ddagger}$ At 4 hours $0 \oplus 0$ $13 (43.33\%)$ $0 (0\%)$ $<0001^{\ddagger}$ No pain $0 (0\%)$ $13 (43.33\%)$ $0 (0\%)$ $<0001^{\ddagger}$ Mild pain $7 (23.33\%)$ $17 (56.67\%)$ $0 (0\%)$ $<0001^{\ddagger}$ Severe pain $23 (76.67\%)$ $0 (0\%)$ $24 (80\%)$ $C \text{ vs N: } 0.0003^{\ddagger}$ Severe pain $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $0 0 0 0 0^{\circ}$ $0 0 0 0^{\circ}$	Severe pain	0(0%)	0(0%)	7 (23.33%)	D vs N: $<.0001^*$
At 4 hours           No pain         0 (0%)         13 (43.33%)         0 (0%)         <.0001*	Mean ± SD	0 ± 0	0 ± 0	$5.8 \pm 1.32$	<.0001 <sup>‡</sup> C vs D: 1 C vs N: <.0001 D vs N: <.0001
No pain $0 (0\%)$ $13 (43.33\%)$ $0 (0\%)$ $<.0001^*$ Mild pain         7 (23.33\%) $17 (56.67\%)$ $0 (0\%)$ $C vs D: <.0001^*$ Moderate pain         23 (76.67\%) $0 (0\%)$ $24 (80\%)$ $C vs N: 0.0003^*$ Severe pain $0 (0\%)$ $0 (0\%)$ $6 (20\%)$ $D vs N: <.0001^*$	At 4 hours				*
Mild pain $7 (23.53\%)$ $17 (56.67\%)$ $0 (0\%)$ C vs D: <.0001'           Moderate pain $23 (76.67\%)$ $0 (0\%)$ $24 (80\%)$ C vs N: $0.0003^*$ Severe pain $0 (0\%)$ $0 (0\%)$ $6 (20\%)$ D vs N: $<.0001^*$	No pain	0 (0%)	13 (43.33%)	0 (0%)	<.0001 <sup>*</sup>
Introductate pair $25 (70.07\%)$ $0 (0\%)$ $24 (80\%)$ C Vs N: $0.0003$ Severe pain $0 (0\%)$ $0 (0\%)$ $6 (20\%)$ D vs N: $<.0001^*$	Mild pain Moderate pair	/ (23.33%)	17 (56.67%)	0(0%)	C vs D: <.0001'
$\mathbf{M} = \left\{ \begin{array}{ccc} 0 & 0 \\ 0 &$	Severe pain	23(10.01%)	0(0%)	24 (00%) 6 (20%)	$D vs N: < 0001^*$
Mean $\pm 5D$   3.23 $\pm 0.86$   0.9 $\pm 0.88$   5.9 $\pm 0.88$   <.0001*	Mean ± SD	$3.23 \pm 0.86$	$0.9 \pm 0.88$	5.9 ± 0.88	<.0001 <sup>‡</sup>

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				C vs D: <.0001
				C vs N: <.0001
				D vs N: <.0001
At 6 hours				*
Moderate pain	26 (86.67%)	30 (100%)	24 (80%)	0.032
	4 (12 220)	0 (00()	C (2001)	C vs D: $0.112$
Severe pain	4 (13.33%)	0(0%)	6 (20%)	C VS N: $0.731$
				D VS IN: 0.024
				$<.0001^{\circ}$
Mean ± SD	$5.07 \pm 1.11$	$4.1\pm0.88$	$5.83 \pm 0.79$	C vs D. 0.0001 C vs N 0.002
				D vs N: $< .0001$
At 8 hours				
Moderate pain	26 (86.67%)	17 (56.67%)	22 (73.33%)	0.034 <sup>†</sup>
•	, , , ,	, , , , , , , , , , , , , , , , , , ,	, , , , , , , , , , , , , , , , , , ,	C vs D: 0.02*
Severe pain	4 (13.33%)	13 (43.33%)	8 (26.67%)	C vs N: 0.333*
-				D vs N: $0.176^{\dagger}$
				$0.022^{\ddagger}$
Mean + SD	$557 \pm 0.73$	$6.13 \pm 0.86$	$5.97 \pm 0.81$	C vs D: 0.007
	5.57 = 0.75	0.15 = 0.00	5.57 = 0.01	C vs N: 0.056
				D vs N: 0.422
At 10 hours	24 (000)	17 (56 670)	22 (76 (79))	
Moderate pain	24 (80%)	1/(56.6/%)	23 (76.67%)	$0.098^{\circ}$
Source pain	6 (20%)	12 (12 220/)	7 (22 220/)	C vs D: $0.052^{\circ}$
Severe pain	0 (20%)	15 (45.55%)	7 (23.33%)	$C VS N. 0.754^{\circ}$
				0.003 <sup>‡</sup>
				$C_{\rm VS} D^{\circ} 0.001$
Mean $\pm$ SD	$5.87 \pm 0.73$	$6.43 \pm 0.5$	$6 \pm 0.69$	C vs N: 0.43
				D vs N: 0.012
At 15 hours				
Moderate pain	22 (73.33%)	14 (46.67%)	21 (70%)	0.065 <sup>†</sup>
				C vs D: $0.055^{\dagger}$
Severe pain	8 (26.67%)	16 (53.33%)	9 (30%)	C vs N: 0.774 <sup>†</sup>
				D vs N: $0.067^{\dagger}$
				0.004*
Mean ± SD	$6.03 \pm 0.72$	$6.57 \pm 0.57$	$6.03 \pm 0.76$	C vs D: 0.004
				C vs N: 1
A 4 10 h				D vs N: 0.004
At 18 nours Moderate pain	18 (60%)	10 (22 220/)	22 (76 670/)	0.002
Woderate pain	18 (00%)	10 (55.55%)	23 (10.01%)	$C vs D 0.03^{\dagger}$
Severe pain	12 (40%)	20 (66 67%)	7 (23 33%)	C vs N: $0.165^{\dagger}$
Severe pull	12(10/0)	20 (00.0770)	7 (20.0070)	D vs N: $0.0007^{\dagger}$
				0.049 <sup>‡</sup>
	6.00 0.61	6.5 0.50	6 0 <b>7</b> 0 64	C vs D: 0.344
Mean $\pm$ SD	$6.33 \pm 0.61$	$6.5 \pm 0.78$	$6.07 \pm 0.64$	C vs N: 0.132
				D vs N: 0.015
At 24 hours				
Moderate pain	14 (46.67%)	8 (26.67%)	22 (73.33%)	0.001 <sup>†</sup>
				C vs D: 0.108 <sup>†</sup>
Severe pain	16 (53.33%)	22 (73.33%)	8 (26.67%)	C vs N: $0.035^{\dagger}$
				D vs N: 0.0003'
				0.001*
Mean ± SD	$6.53 \pm 0.51$	$6.73 \pm 0.45$	$6.27\pm0.45$	C vs D: 0.103
				$C_{VS}$ IN: 0.031 D vs N: 0.0002
	1	1	1	$\mathbf{I}$ $\mathbf{I}$ $\mathbf{J}$ $\mathbf{V}$ $\mathbf{S}$ $\mathbf{I}$ $\mathbf{N}$ $\mathbf{U}$ $\mathbf{U}$ $\mathbf{U}$ $\mathbf{U}$ $\mathbf{U}$

\* Fisher's exact test, <sup>†</sup> Chi square test, <sup>‡</sup> ANOVA

All patients had no pain at 0 minute, 2 minutes, 5 minutes, 10 minutes, 20 minutes, 30 minutes, 45 minutes.

Severity of pain was significantly higher in group N at 60 minutes, at 90 minutes, at 120 minutes, at 180 minutes, at 4 hours as compared to group C and D. No significant difference was seen in severity of pain between group C and D at 60 minutes, at 90 minutes, at 120 minutes, at 180

minutes. Severity of pain was significantly higher in group C as compared to group D at 4 hours.

Severity of pain was significantly higher in group N at 6 hours as compared to group D (p value=0.024). No significant difference was seen in severity of pain between group C and D (p value=0.112) and between group C and N (p value=0.731) at 6 hours.

Severity of pain at 8 hours was significantly higher in group D as compared to group C (p value=0.02) and was comparable between group C and N (p value=0.333) and between group D and N (p value=0.176).

Severity of pain at 10 hours (p value=0.098), at 12 hours (p value=0.065) was comparable between group C, D and N.

Severity of pain at 18 hours was higher in group D as compared to group N (p value=0.0007), group C (p value=0.038).

Severity of pain at 18 hours was comparable between group C and N. (p value=0.165)

Severity of pain at 24 hours was significantly lower in group N as compared to group C (p value=0.035) and D (p value=0.0003). Severity of pain at 24 hours was comparable between group C and D. (p value=0.108)

Table 4: Comparison of post ope	erative demand of	rescue analgesia	between group C	, D and N
Post operative demand of rescue analgesia	Group C (n=30)	Group D (n=30)	Group N (n=30)	P value
At 0 minute				
No	30 (100%)	30 (100%)	30 (100%)	NA
At 2 minutes				
No	30 (100%)	30 (100%)	30 (100%)	NA
At 5 minutes				
No	30 (100%)	30 (100%)	30 (100%)	NA
At 10 minutes		•		
No	30 (100%)	30 (100%)	30 (100%)	NA
At 20 minutes				
No	30 (100%)	30 (100%)	30 (100%)	NA
At 30 minutes				
No	30 (100%)	30 (100%)	30 (100%)	NA
At 45 minutes				
No	30 (100%)	30 (100%)	30 (100%)	NA
At 60 minutes				
No	30 (100%)	30 (100%)	29 (96.67%)	1*
				C vs D: NA
Yes	0 (0%)	0 (0%)	1 (3.33%)	C vs N: $1^*$
				D vs N: 1 <sup>*</sup>
At 90 minutes				
No	30 (100%)	30 (100%)	5 (16.67%)	$<.0001^{\dagger}$
				C vs D: NA
Yes	0 (0%)	0 (0%)	25 (83.33%)	C vs N: <.0001 <sup>*</sup>
				D vs N: <.0001*
At 120 minutes				
No	30 (100%)	30 (100%)	4 (13.33%)	$< .0001^{\dagger}$
				C vs D: NA
Yes	0 (0%)	0 (0%)	26 (86.67%)	C vs N: <.0001
				D vs N: <.0001
At 180 minutes	20 (1000()	20 (1000()	0 ( ( ( ( ( ( ( ( ( ( ( ( ( ( ( ( ( ( (	0001
No	30 (100%)	30 (100%)	2 (6.67%)	<.0001
X7	0 (00()	0 (00()	29 (02 220/)	C vs D: NA
Yes	0(0%)	0(0%)	28 (93.33%)	C VS N: <.0001
A.4. 4 h arrows				D VS IN: <.0001
At 4 hours	7 (22 220/)	20 (100%)	0(00/)	< 0001 <sup>†</sup>
110	7 (23.33%)	30 (100%)	0(0%)	$< 0.0001^{\circ}$
Vas	23 (76 67%)	0 (0%)	30 (100%)	C vs D. < .0001
105	23 (10.0170)	0(070)	50 (10070)	$D vs N < 0.011^*$
At 6 hours				D 1311. (.0001
Yes	30 (100%)	30 (100%)	30 (100%)	NA
At 8 hours	50 (10070)	50 (10070)	50 (10070)	1111
Yes	30 (100%)	30 (100%)	30 (100%)	NA
At 10 hours	20 (100/0)	20 (100/0)	20 (100/0)	4 14 <b>4</b>
Yes	30 (100%)	30 (100%)	30 (100%)	NA
At 15 hours	20 (100/0)	20 (100/0)	20 (100/0)	4 14 <b>4</b>
Yes	30 (100%)	30 (100%)	30 (100%)	NA
At 18 hours	30 (10070)	50 (100/0)	55 (10070)	11/1
Yes	30 (100%)	30 (100%)	30 (100%)	NA
1.00	50 (100/0)	50 (100/0)	55 (100/0)	11/1
At 24 hours				
At 24 hours	30 (100%)	30 (100%)	30 (100%)	NA

\*Fisher's exact test, <sup>†</sup> Chi square test

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None of the patient demanded rescue analgesia at 0 minute to 45 minutes. All patients demanded rescue analgesia from 6 to 24 hours.

Demand for rescue analgesia was comparable between group C, D and N at 60 minutes (p value=1).

Demand for rescue analgesia was significantly higher in group N as compared to group C and D at 90, 20, 180 minutes and 4 hours.

At 4 hours, demand for rescue analgesia was significantly higher in group C as compared to group D. (p value<.0001)

# 4. Discussion

In our study the mean time taken for onset of sensory block is  $2.6\pm0.6$ mins in the control group,  $1.5\pm0.5$ mins in the clonidine group and  $1.2\pm0.379$ mins in the dexmedetomidine group. There is a statistically significant decrease in the onset of sensory blockade in clonidine group and in the dexmedetomidine group compared to the control group.

The studies conducted by Sarma J et al <sup>7</sup>, Solanki SL et al <sup>8</sup>Mahendru V et al<sup>9</sup> and Zang C et al<sup>10</sup>, authors also observed a significant reduction in the onset time of sensory blockade.

The time taken for sensory block to regress to S1 in the present study is190.13 $\pm$ 27.44 mins in the control group, 343.27 $\pm$ 24.64 mins in the clonidine group and 366.16 $\pm$ 36.55 mins in the dexmedetomidine group. There is a statistically significant increase in the total duration of sensory blockade in clonidine group and dexmedetomidine group compared to the control group. (P<0.05).

In studies conducted by Kanazi GE et al <sup>11</sup>, Sarma J et al <sup>7</sup>, Solanki SL et al <sup>8</sup>, Mahendru V et al <sup>8</sup> and Zang C et al <sup>10</sup> authors observed statistically significant longer duration of sensory blockade in dexmedetomidine and clonidine groups as compared to control group.

In our study the mean time for onset of motor block is  $3.9\pm0.7$  mins in control group,  $1.7\pm0.46$  mins in clonidine group and  $1.26\pm0.44$  mins in dexmedetomidine group. There is a statistically highly significant decrease in the mean time for onset of motor blockade in the dexmedetomidine group and clonidine group compared to the control group.

In studies conducted by Kanazi GE et al <sup>11</sup>, Sarma J et al <sup>7</sup>, Solanki SL et al <sup>8</sup>, Mahendru V et al <sup>9</sup>and Zang C et al <sup>10</sup> authors observed a significant decrease in the mean time for onset of motorblockade which correlates with our study.

In our study the mean duration of motor blockade was  $164.27\pm24.05$  mins in control group,  $280.77\pm24.22$  mins in clonidine group and  $303.33\pm33.73$  mins in dexmedetomidine group. There is a statistically highly significant increase in the duration of motor blockade in dexmedetomidine group and clonidine group compared to the control group.

In studies conducted by Kanazi GE et al <sup>11</sup>, Sarma J et al <sup>7</sup>, Solanki SL et al <sup>8</sup>, Mahendru V et al <sup>9</sup> and Zang C et al <sup>10</sup>

authors observed a significant increase in the duration of motor blockade.

# 5. Future Scope

Adjuvants are used along with hyperbaric bupivacaine in spinal anaesthesia to prolong the duration of analgesia. Combining alpha agonists like clonidine and dexmedetomidine with hyperbaric bupivacaine can significantly shorten the onset of sensory and motor effect and increase the duration of action. Hence, can help in better regional anaesthesia.

# 6. Conclusion

We concluded that the supplementation of bupivacaine with dexmedetomidine  $5\mu g$  or clonidine  $50\mu g$  in spinal anaesthesia produces significant shorter on set of motor and sensory block with longer duration of sensory and motor block when compared to bupivacaine alone. The 50  $\mu g$  of clonidine or 5  $\mu g$  dexmedetomidine dose provides maximum benefit with minimum side effects. These doses have minimal effect on sedation level, heart rate and mean arterial pressure without requiring any therapeutic intervention and hence can be advocated as an adjuvant to bupivacaine in spinal anaesthesia for lower limb surgeries. Amongst dexmedetomidine and clonidine, dexmedetomidine shows significantly longer duration of analgesia than clonidine which proves it to be better adjuvant than clonidine at the mentioned dose.

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