



A Comparative Study to Evaluate the Post Operative Analgesia Comparing Dexmedetomidine and Clonidine with Epidural Levobupivacaine for Pelvis and Lower Limb Orthopaedic Surgeries

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Abstract

Background: Alpha 2 agonists are being used as adjuvants in epidural analgesia as they lead to analgesia, anxiolysis and sedation.

Aim: This study aims to evaluate the post operative analgesic effects of epidural dexmedetomidine and clonidine with 0.125%levobupivacaine

Methods: A comparative study was done to assess the efficacy and clinical profile of two α_2 adrenergic agonists – clonidine and dexmedetomidine administered epidurally in combination with intrathecal 0.125%levobupivacaine. The study was conducted for 1 year. Sixty adult patients ASA-PS Class I and II undergoing pelvis and lower limb orthopaedic surgery were randomly assigned into two groups, to receive either epidural dexmedetomidine (1 μ g/kg) or clonidine (2 μ g/kg) with 0.125% isobaric levobupivacaine.

Results: Dexmedetomidine provided a prolonged analgesia, as evidenced by the distribution of VAS scores and requirement rescue analgesic among two groups.

Keywords: Epidural analgesia, 0.125%Levobupivacaine, Dexmedetomidine, Clonidine.

Introduction

It has been hypothesized that epidural anaesthesia lessens the perioperative stress and works on careful result of surgical success by relieving the pain. Artistic proof has set up the safety of levobupivacaine over bupivacaine when utilized in epidural anaesthesia as the rate of different unfavourable outcome is higher with the last when compared with levobupivacaine.

As an amide local anaesthetic, the activity and pharmacodynamics of levobupivacaine are like

those of bupivacaine. It applies its effects through reversible blockade of neuronal sodium channels. Myelinated nerves are obstructed through exposure at the nodes of Ranvier more promptly than unmyelinated nerves; and small nerves are impeded more effectively than large nerves. Levobupivacaine is lipid solvent and exceptionally protein bound. The PKa of levobupivacaine is like that of bupivacaine and ropivacaine; however higher than that of lignocaine. Its higher lipid-solvency makes it

more powerful which brings about a longer duration of action.

Alpha-2 adrenergic agonists have both pain relieving and narcotic properties when utilized as an adjuvant in local sedation. They have been accounted for to work on the improved epidural sedation. The sedative and the pain relieving necessity gets diminished to a greater degree by the utilization of these two adjuvants on account of their pain relieving properties and augmentation of local anaesthetic effects as they cause hyperpolarization of nerve tissue by modifying transmembrane potential and particle conductance at locus coeruleus in the brainstem. These medications cause negligible respiratory depression when utilized as adjuvants to local sedation.

Aim and Objective

The present comparative study aims at comparing the haemodynamic, sedative and analgesia potentiating effects of epidurally administered clonidine and dexmedetomidine when combined with 0.125% Levobupivacaine epidurally in patients undergoing pelvis and lower limb orthopaedic surgeries.

Materials and Methodology

Inclusion Criteria

- Sixty individuals who had been admitted for pelvis & lower limb orthopedic surgeries, in the age Group of 18 - 60 years in the ASA I and II grade were included.

Exclusion Criteria

- Known allergic patients to local anaesthetics, Clonidine & Dexmedetomidine
- Patient refusal
- Infection at the local site of injection
- Haematological disease
- coagulopathies
- psychiatric diseases
- second- or third-degree heart block
- renal and hepatic insufficiency

- uncontrolled diabetes and hypertension
- history of drug abuse

Study Design

Patients were split into two groups, 30 patients in each of Clonidine group and Dexmedetomidine group randomly.

Study Method

Under stringent aseptic precautions affected person in sitting position, epidural space displaying utilizing 18G Tuohy needle with loss of resistance method at L2 L3 inter vertebral space. Once the epidural room was revealed, epidural catheter was placed and four cm length of catheter placed within the area. A test dose serving of 3ml of 1.5 % lignocaine with 15µg adrenaline was provided. Right after excluding inadvertent subarachnoid or maybe intravascular positioning of catheter, Sub-arachnoid block was carried out at L3 - L4 Intervertebral space by using 23G Quincke Babcock's spinal needle. 3ml of Inj. Bupivacaine 0.5 % (heavy) was injected into the subarachnoid space. Patient positioned in supine position carefully. If the sensory blockade reached T10 level, surgery was commenced. Intra operatively pulse rate, respiratory rate, blood pressure, saturation (SpO₂), urine output had been monitored. Following the surgery, patient was shifted to ICU for post operative pain control. In the ICU, post operative epidural analgesia was provided in the serving of Inj. Levobupivacaine 0.125% 8 ml volume with dexmedetomidine 1µg /ml in one group and other group received inj. Levobupivacaine 0.125% 8ml volume with clonidine 2mcg/ml of epidural analgesic supplementation and patients were monitored.

Variables Observed

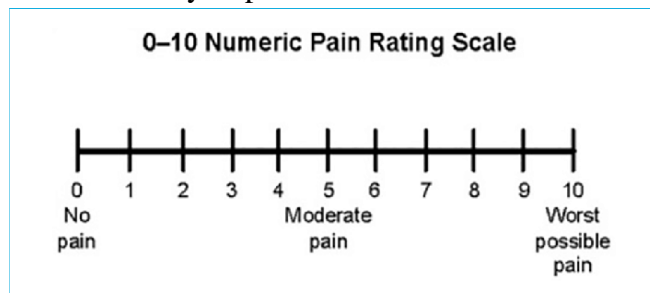
- 1) Time to achieve T10 sector sensory block - after time of subarachnoid block to loss of pin prick sensation at T10
- 2) 2 segment regression time in subarachnoid block (in minutes) - time period to regress sensation to pin prick 2 sections from the

top degree of blockade.

- 3) Time to need very first epidural top up since time of subarachnoid block performed (when VAS score > 5)
- Total number of epidural supplementations
- Time interval between each epidural analgesic supplementation
- Side effects like dizziness, headache, nausea, vomiting, ataxia, bradycardia

Visual analogue pain score

Individuals have been asked to draw the effort on the ten point visible analogue scale of Pain based on the intensity of pain. It was noticed each hour

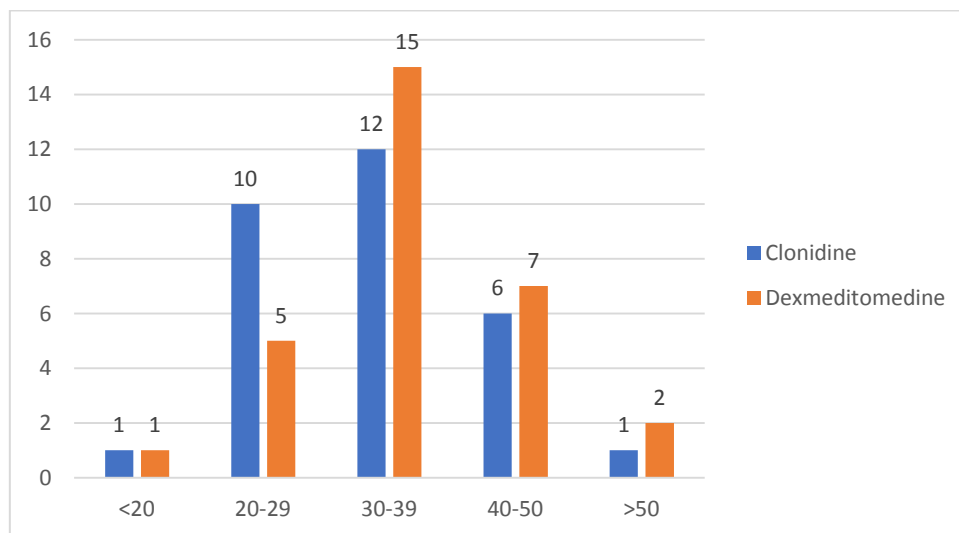


Observation and Results

Age of the Study Population

More individuals from both the clonidine and dexmedetomidine group falls under age group of 30-39 with 40% each respectively.

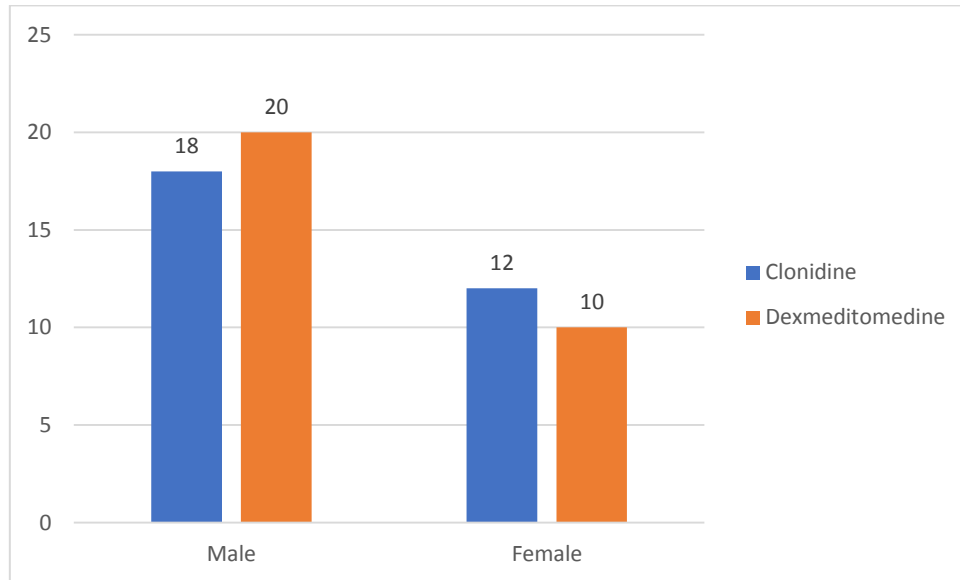
Age Group					
Parameters	Clonidine		Dexmedetomidine		Grand Total
	Frequency	Percentage	Frequency	Percentage	
<20	1	3.33	1	3.33	2
20-29	10	33.33	5	16.67	15
30-39	12	40.00	15	50.00	27
40-50	6	20.00	7	23.33	13
>50	1	3.33	2	6.67	3
Grand Total	30	100.00	30	100.00	60



Sex of the Study Population

Both groups had more males as the participants for the study.

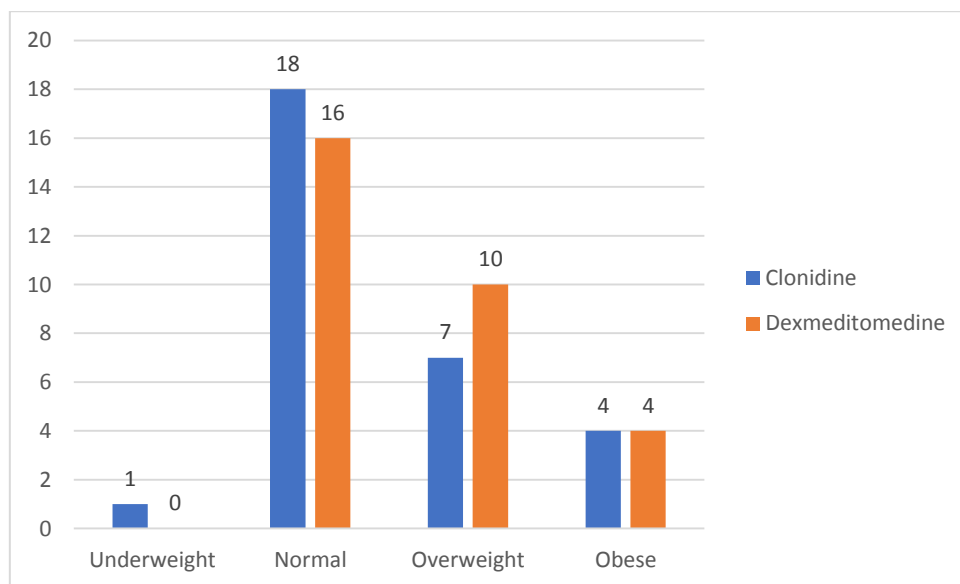
Sex					
Parameters	Clonidine		Dexmedetomidine		Grand Total
	Frequency	Percentage	Frequency	Percentage	
Male	18	60.00	20	66.67	38
Female	12	40.00	10	33.33	22
Grand Total	30	100.00	30	100.00	60



BMI of the study groups:

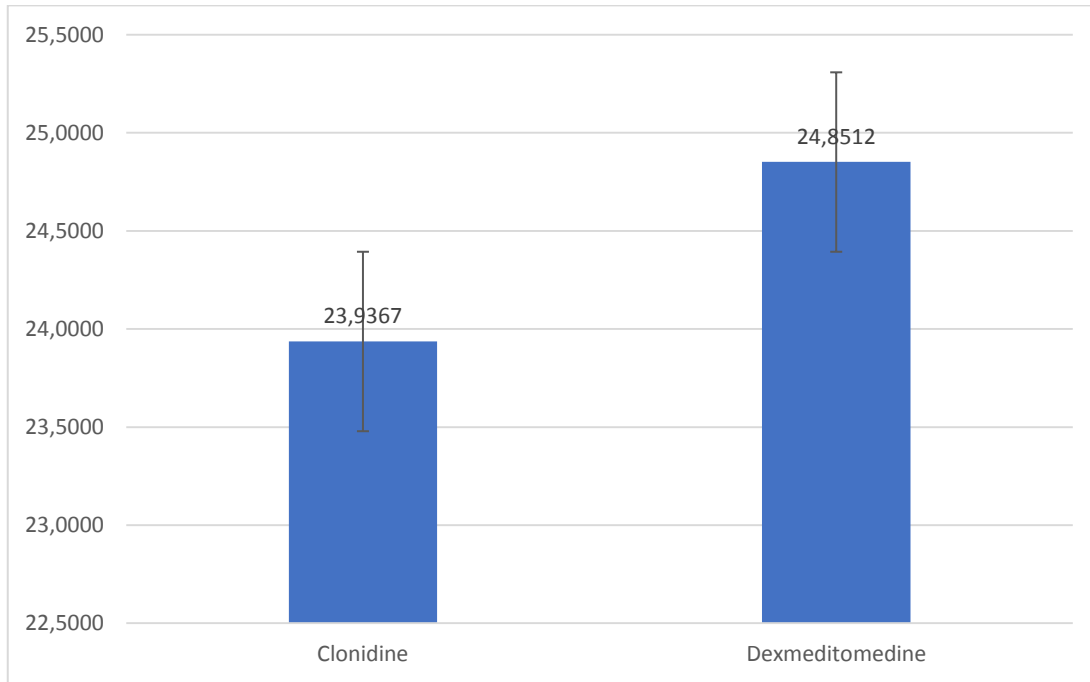
Both the groups had individuals being normal in weight, 60% among the clonidine group while 53.33% among dexmedetomidine group.

BMI					
Parameters	Clonidine		Dexmedetomidine		Grand Total
	Frequency	Percentage	Frequency	Percentage	
Underweight	1	3.33	0	0.00	1
Normal	18	60.00	16	53.33	34
Overweight	7	23.33	10	33.33	17
Obese	4	13.33	4	13.33	8
Grand Total	30	100.00	30	100.00	60



Mean BMI of the clonidine and dexmedetomidine groups are 23.93 & 24.85 mean values respectively.

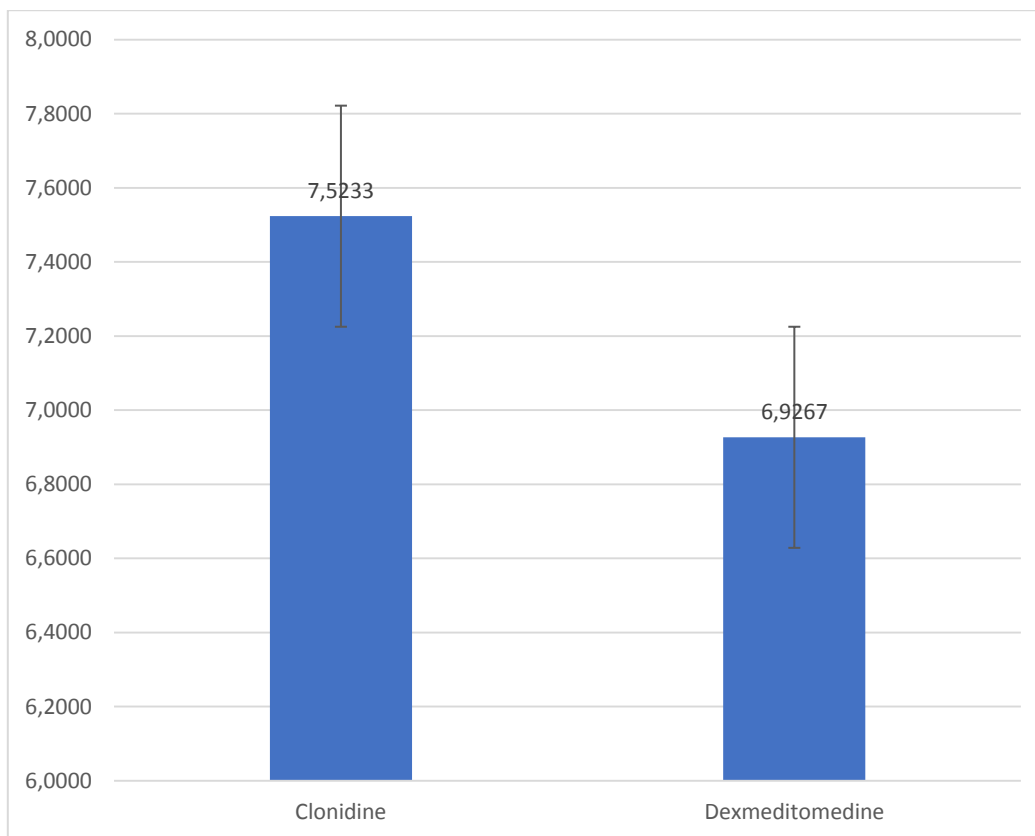
BMI			
	Mean	Standard Deviation	p value
Clonidine	23.9367	4.2172	0.4163
Dexmedetomidine	24.8512	4.4333	



Onset of analgesia

Onset of analgesia is earlier for dexmedetomidine group with mean of 6.9 while clonidine has 7.5 and it seemed to be statistically significant.[1,7]

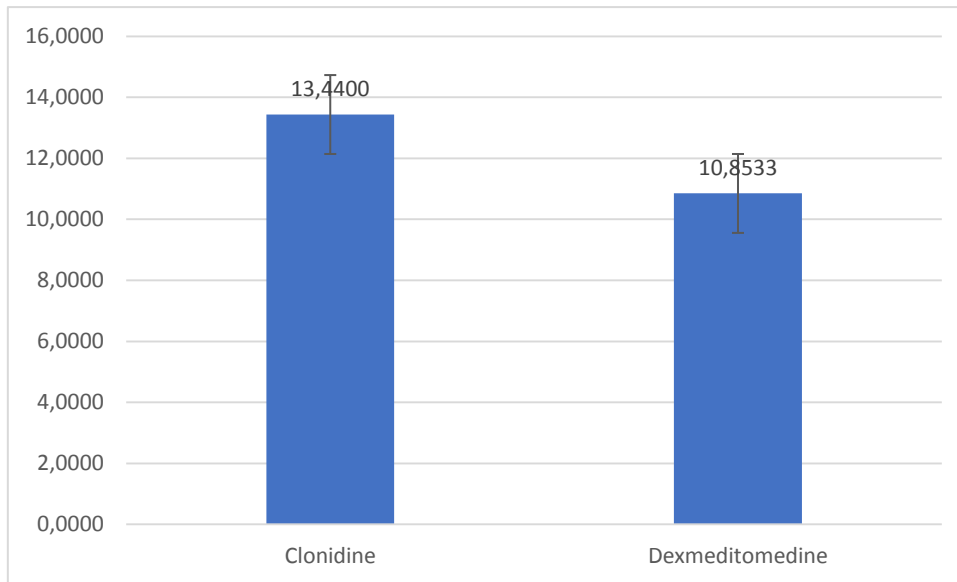
Onset of analgesia			
	Mean	Standard Deviation	p value
Clonidine	7.5233	1.2781	0.0406
Dexmedetomidine	6.9267	0.8952	



Time of peak onset of analgesia

The peak onset of analgesia is found to earlier in the dexmedetomidine group (mean of 10.85) than the clonidine group.^[2,5]

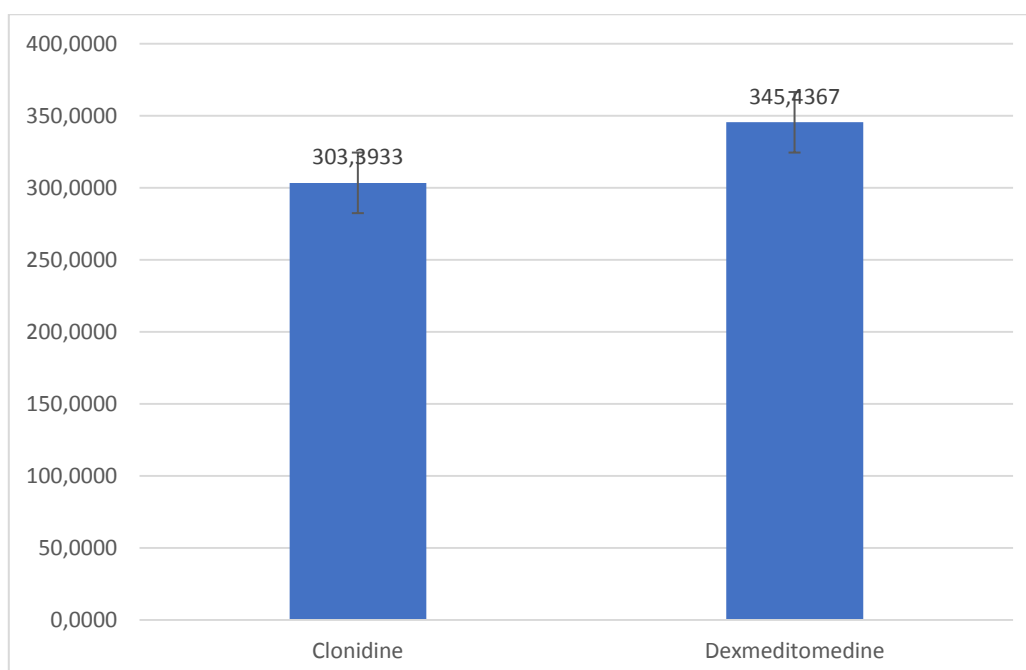
Time of peak onset of analgesia			
	Mean	Standard Deviation	p value
Clonidine	13.4400	1.0944	0.0000
Dexmeditomedine	10.8533	1.3472	



Duration of analgesia

The average time duration of analgesic effect is more for the dexmedgroup (mean value of 345.44 minutes) compared with the (mean value of 303.39 minutes) in the clonidine group.^[6]

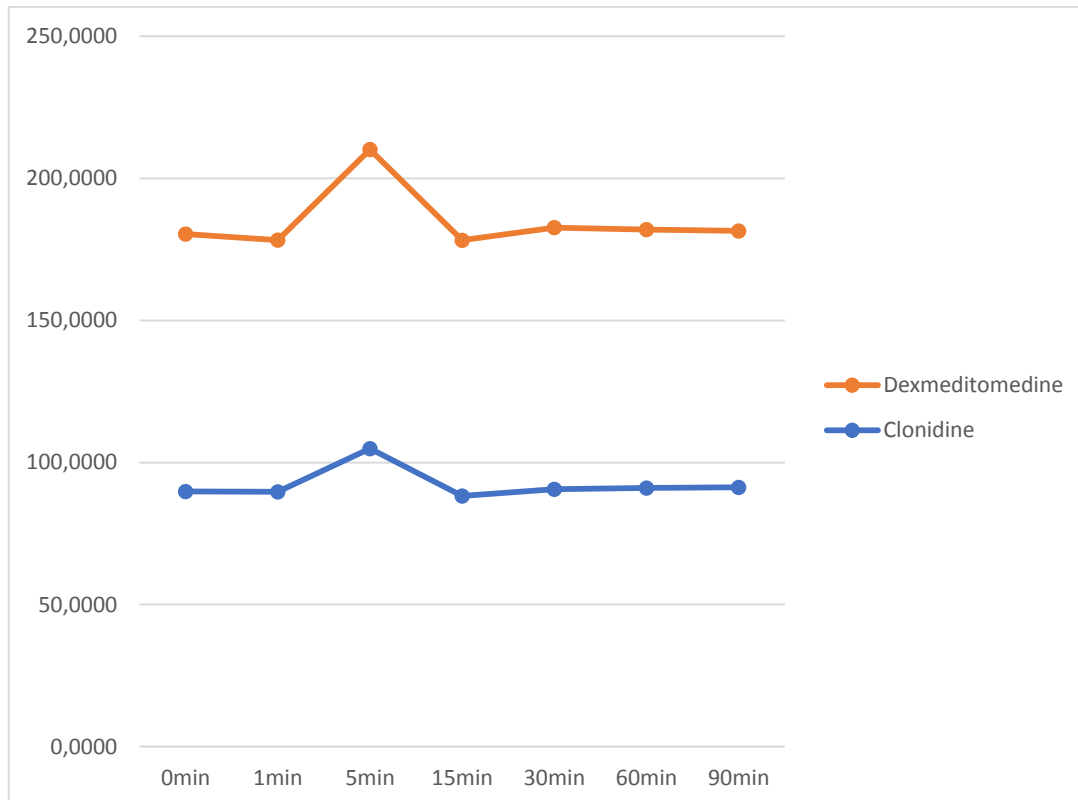
Duration of analgesia			
	Mean	Standard Deviation	p value
Clonidine	303.3933	19.3684	0.0000
Dexmeditomedine	345.4367	21.5832	



Mean heart rate during the procedure:

Initially around the 5 minute mark mean heart rate seems to go past 100 for both the groups.

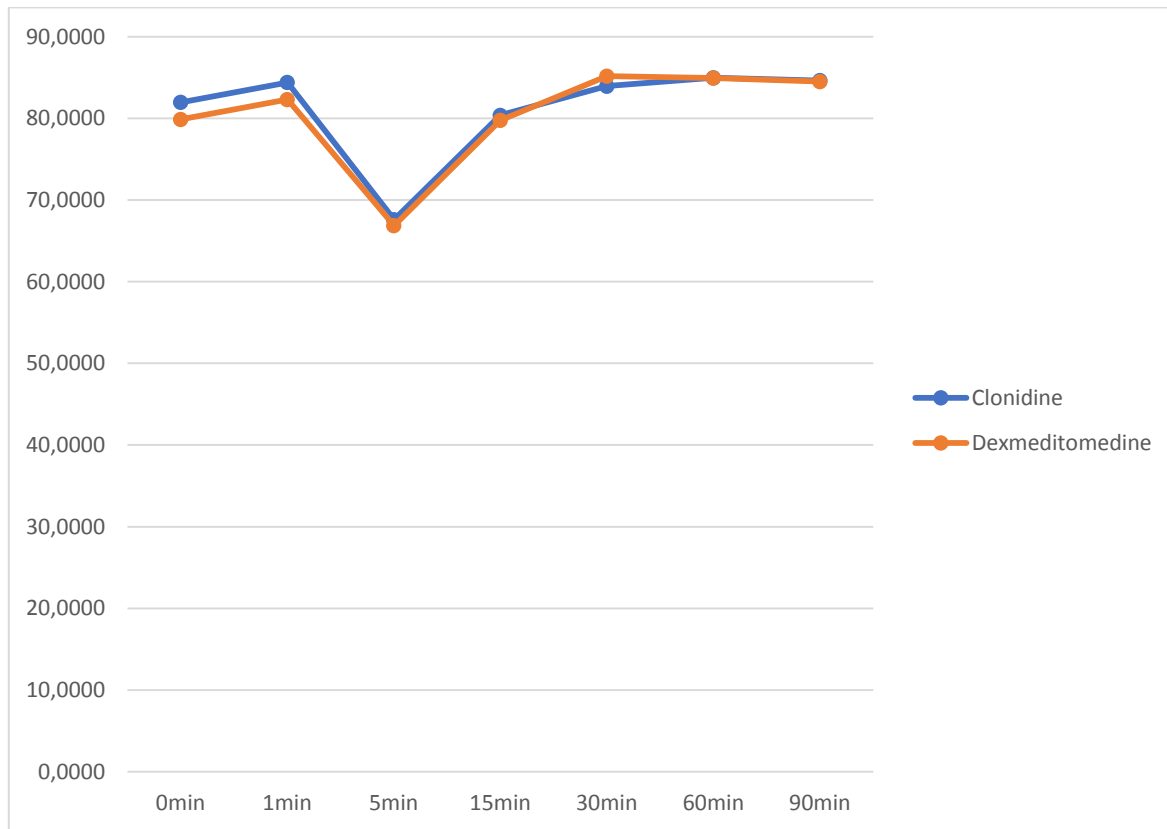
Heart Rate					
Parameters	Clonidine		Dexmeditomedine		p value
	Mean	Standard Deviation	Mean	Standard Deviation	
0min	89.7667	5.8996	90.6000	6.5422	0.6063
1min	89.6667	5.2479	88.5667	6.3500	0.4675
5min	104.8667	3.1811	105.2333	2.8850	0.6418
15min	88.2000	5.8333	89.9667	6.1671	0.2590
30min	90.5667	5.7994	92.0667	6.3078	0.3416
60min	91.0000	6.6332	90.9333	6.3023	0.9683
90min	91.2333	5.7457	90.2000	6.0992	0.5021



Mean Systolic blood pressure during the procedure:

Higher blood pressure readings at the earlier phases and lower values as the effect gets more enhanced is the trend seen in both the groups.[3,4]

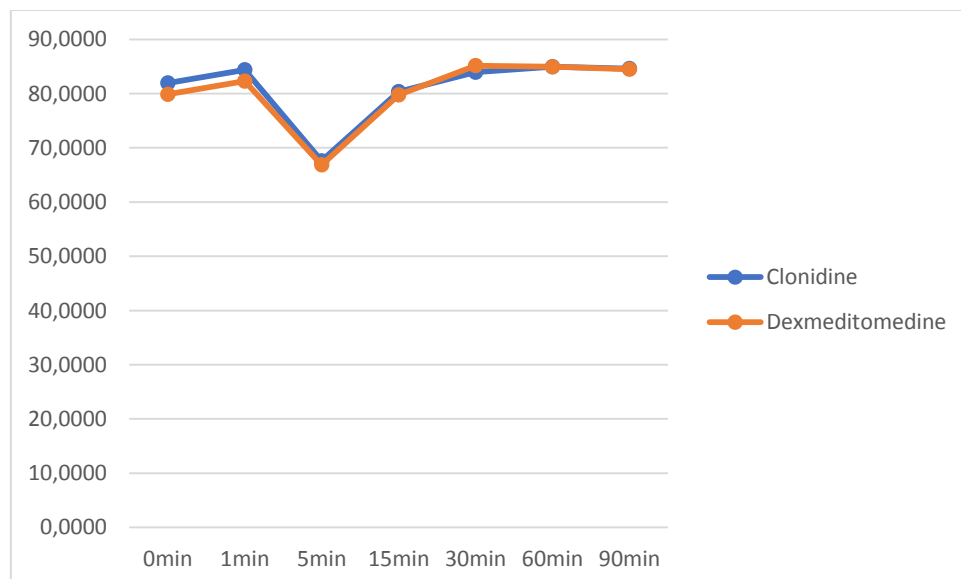
SBP					
Parameters	Clonidine		Dexmeditomedine		p value
	Mean	Standard Deviation	Mean	Standard Deviation	
0min	120.4000	5.5124	118.0000	5.9364	0.1101
1min	114.6667	2.8808	115.4333	2.8969	0.3083
5min	94.6000	3.0126	94.9000	2.9048	0.6960
15min	104.6000	3.1028	105.4000	3.1250	0.3239
30min	108.1333	5.8353	110.8333	5.2920	0.0655
60min	113.8667	2.6226	113.9667	2.7478	0.8858
90min	109.2667	7.0854	109.2000	6.5464	0.9699



Mean diastolic blood pressure during the procedure:

Higher blood pressure readings at the earlier phases and lower values later in both the groups.^[8]

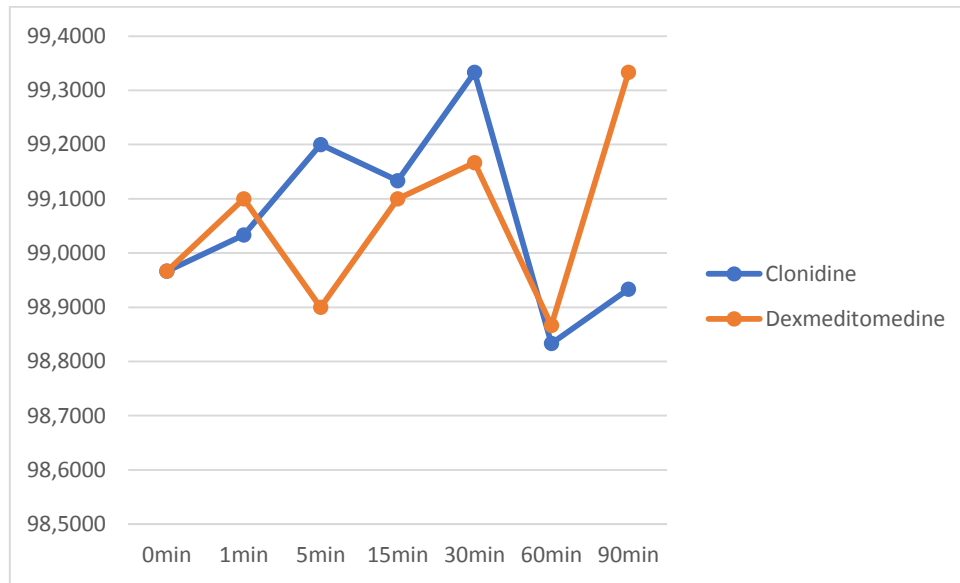
DBP					
Parameters	Clonidine		Dexmedetomidine		p value
	Mean	Standard Deviation	Mean	Standard Deviation	
0min	81.9667	6.1222	79.8667	5.9465	0.1830
1min	84.4000	4.0052	82.3000	4.4268	0.0589
5min	67.6000	4.6505	66.8667	4.4855	0.5366
15min	80.3667	2.9300	79.7667	2.7628	0.4178
30min	83.9333	3.3624	85.1667	3.4148	0.1640
60min	84.9667	3.3060	84.9333	3.3521	0.9692
90min	84.6333	3.2215	84.5000	2.9449	0.8677



SPo2 during the procedure:

The mean Spo2 is steady throughout the procedure in both the groups.

SPO2					
Parameters	Clonidine		Dexmeditomedine		p value
	Mean	Standard Deviation	Mean	Standard Deviation	
0min	98.9667	0.8899	98.9667	0.7649	1.0000
1min	99.0333	0.8899	99.1000	0.8847	0.7721
5min	99.2000	0.7611	98.9000	0.7589	0.1317
15min	99.1333	0.8193	99.1000	0.8847	0.8802
30min	99.3333	0.7581	99.1667	0.7915	0.4083
60min	98.8333	0.8339	98.8667	0.7761	0.8732
90min	98.9333	0.8683	99.3333	0.7112	0.0558



Discussion

Outcomes of this particular prospective, randomized, double blinded analysis show that inclusion of 1µg/kg dexmedetomidine to 0.125 % Levobupivacaine creates longer period of analgesia when compared with inclusion of 2µg/kg weight of clonidine to 0.125 % levobupivacaine epidurally for postoperative analgesia. Inclusion of dexmedetomidine to levobupivacaine likewise hastens the coming of analgesia and raises sedation score.

Control of postoperative pain constitutes a significant issue for doctors that take care of postoperative patients. Additionally, good control of postoperative pain is vitally important to reduce numerous pulmonary, metabolic, and mental complications.^[9] Many scientific studies have indicated the usage of postoperative epidural analgesia in complications are reduced by high-risk patients to a much better extent.^[10]

Many scientific studies show that epidural analgesia with local anaesthetics coupled with opioid allows for far better postoperative analgesia compared to systemic opioid or epidural analgesia by itself which improves the surgical outcome.^[11,12] Nevertheless, the usage of neuraxial opioids was related to a number of side effects, therefore different choices like α2 agonists are being thoroughly examined as a substitute with focus on opioid related side effects such as for instance respiratory depression, urinary retention, nausea, then pruritus.^[17] The utilization of α2agonists for regional neural blockade in conjunction with local anaesthetic leads to improved duration of sensory blockade without any distinction in onset time.

Bupivacaine is popular medication within epidural anaesthesia, though numerous researches has recognized the severe negative effects serotonin and concern about therapy resistant aerobic

toxicity with bupivacaine which resulted in the launch of the newer representative levobupivacaine (S enantiomer of bupivacaine). Levobupivacaine, a long acting enantiomerically fresh (S enantiomer) amide-type nearby anaesthetic, exerts the pharmacological action of its via reversible blockade of neuronal salt routes with a medical profile much like which of bupivacaine.^[13] Levobupivacaine with the safe pharmacological profile of its, minimal main nervous system as well as cardiac toxicity, differential neuraxial blockade with preservation of engine perform at concentrations that are low (0.125 %), compatibility with α_2 agonists has become turning into a crucial choice for local anaesthesia and analgesia.

In the current study, the hypothesis is the fact that dexmedetomidine became a much better neuraxial adjuvant to levobupivacaine in comparison with clonidine for offering early onset and extended postoperative epidural analgesia and healthy cardiorespiratory parameters.^[19]

A report by Saravana Babu et al. realized that epidural route offers appropriate analgesia in the postoperative period.^[14] Dexmedetomidine is a much better neuraxial adjuvant to ropivacaine in comparison with clonidine for offering early onset and stable cardiorespiratory parameters and prolonged postoperative analgesia. This particular analysis is in total agreement with the study of ours wherein beginning of analgesia (7.26 ± 0.96 compared to 7.96 ± 0.85) was previously in Dexmed group. Duration of analgesia is extended with Dexmed group in comparison with clonidine group (405.6 ± 20.32 vs. 347.9 ± 15.05), with healthy cardiorespiratory parameters in dexmedetomidine team. Sedation was statistically and better significant in Dexmed group at thirty min (1.64 ± 0.48 vs. 1.36 ± 0.48) as well as one h (2.18 ± 0.38 vs. 1.96 ± 0.19) in comparison with clonidine group.^[21]

Bajwa SJ et al. conducted a randomized and prospective research which included fifty adult female individuals between age of forty four as well as sixty five years of ASA bodily Classes I

and II who underwent vaginal hysterectomies.^[15] Group RD got 17ml of 0.75 % epidural ropivacaine along with $1.5\mu\text{g}/\text{kg}$ of dexmedetomidine, while Group RC received admixture of seventeen ml of 0.75 % ropivacaine as well as $2\mu\text{g}/\text{kg}$ of clonidine. They found that inclusion of dexmedetomidine to ropivacaine led to earlier beginning of sensory analgesia at T10 as compared to inclusion of clonidine which is the same result we got in our group.^[20]

Sedation score of dexmedetomidine was statistically and better substantial compared to that of clonidine; the mean time for 2 segment regression as well as motor blockade had been extended in dexmedetomidine team.^[18] Moreover, time for original recovery analgesia was substantially prolonged with dexmedetomidine class when as opposed with the clonidine group. They realized that dexmedetomidine is a much better adjuvant compared to clonidine wearing epidural anaesthesia as much as affected person comfort, healthy cardiorespiratory parameters, intraoperative, and postoperative analgesia are concerned.^[22]

From the study of ours, dexmedetomidine is a much better neuraxial adjuvant compared to clonidine in supplying healthy hemodynamic parameters with much better & statistically significant sedation amounts at thirty min as well as one h and extended postoperative analgesia 405.6 ± 20.32 vs. 347.9 ± 15.05).

Oriol-López and Maldonado-Sánchez conducted a prospective study in 40 patients who were subjected to abdominal surgery under epidural anaesthesia.^[16] They were given epidural dexmedetomidine at a dose of $1\mu\text{g}/\text{kg}$ plus lidocaine and epinephrine at $3-4\text{ mg}/\text{kg}$. The obtained sedation amount, based on Ramsey, at five min was of three, and also it had been of 3 4 from fifteen to ninety min, in ninety % of the public. They realized that ample sedation (Ramsay sedation level of 3 4, $P = 0.05$) was maintained between ten along with 120 min thanks to one bolus epidural serving of dexmedetomidine.

Limitation

Limitation of our study is that we had no placebo group and further scope will be to design the study with different doses of α_2 agonists.

Conclusion

We finally determine and conclude that dexmedetomidine 1 μ g/kg is a much better neuraxial adjuvant to levobupivacaine 0.125 % in comparison with clonidine 2 μ g/kg for offering early onset and extended postoperative epidural analgesia with healthy cardiorespiratory parameters for pelvis & lower limb orthopaedic surgeries.

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