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Comparison of Efficacy of Dexmedetomidine with Clonidine inCombined Spinal Epidural Anesthesia: A Randomized Controlled Study

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Abstract:
Background*: Epidural anesthesia is a versatile technique used for providing anaesthesia and analgesia duringpostoperative period. Alpha 2 adrenergic agonists like clonidine, enhances local anestheticdrugs' action on administration via intrathecal or epidural route. Dexmedetomidine a newer agonist of alpha 2 adrenergic receptors have 8 times more selective α2 adrenoreceptor agonist property comparedto clonidine and hence allows usage of a higher dose of the drug with less alpha-1 effect. The aim of the study is to compare the efficacy of dexmedetomidine with clonidine as adjuvants.*
Materials and Methods*: In this randomized controlled study, 60 patients of ASA physical status I and II to age group of 18-65 years undergoing lower extremity and lower abdominal elective surgeries were included. Patients were randomized into 2 groups.Patients in Group C received clonidine and patients in group D received Dexmedetomidine. Onset, duration of anesthesia, quality of analgesia, hemodynamic parameters, and side effects were assessed and compared between two groups.*
Results*: There was no significant difference in the mean age and gender between two groups. There was no significant difference in the incidence of side effects and quality of analgesia between two groups. But there was significant difference in the onset and duration of analgesia.There was no significant difference in mean heart rate and mean arterial pressure between both groups.*
Conclusion: *We conclude that the addition of 1mcg/kg Dexmedetomidine as an adjuvant to 0.75% Ropivacaine in epidural anesthesia causes an early onset and prolonged duration of sensory analgesia in comparison to 1mcg/kg Clonidine. Epidural dexmedetomidine causes better sedation as compared to Clonidine.*
Key Word*: Dexmedetomidine, clonidine, combined spinal epidural anesthesia, adjuvants, pain*

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I. Introduction

Pain is a dehumanizing experience that destroys the soul and mental harmony. Pain has been a significant problem since its beginning, and it's been a prime concern to put efforts to understand and control it.The International Association for Study of Pain defines pain as "An unpleasant sensory &emotional experience linked with actual or potential tissue damage." This definition compares the interplay between the objective, physiologic sensory aspects of pain and its subjective, emotional, and psychological components.

Epidural anesthesia is a versatile technique used for providing anaesthesia and analgesia in post-operative period. It may be combined with regional anesthesia or other forms of general anesthesia. It can provide intraoperative hemodynamic stability and has been proven to reduce perioperative stress response, thus causing a reduction in complications.

Alpha 2 adrenergic agonists like clonidine enhance the local anesthetic drugs' action on administration through intrathecal or epidural route. It acts by causing blockade of the A and C fibers leading to local vasoconstriction, decreasing the intensity and duration of analgesia. It causes sedation, bradycardia and hypotension.[1-2]Dexmedetomidine, a newer agonist of alpha 2 adrenergic receptors has 8 times more selective α2 adrenoreceptor agonist property compared toclonidine and hence allows using higher dose with less alpha-1 effect. It shows hemodynamic stability, analgesic, anxiolytic, sedative, neuroprotective, and anaesthetic-sparing effects. It causes intense motor blockade and sedation without causing any increase in the incidence of adverse effects.[3-12]

Since studies on comparison of dexmedetomidine with clonidine are less in India, the current study was undertaken.

Aim: To compare the effects of clonidine versus dexmedetomidine added as an adjuvant to Ropivacaine for patients undergoing lower abdominal and limb surgeries under combined spinal epidural anesthesia (CSEA).

II. Materials And Methods

This randomized controlled double-blind study was carried out in the Department of anesthesia at a tertiary care center named Maharaja Institute of medical sciences, Vizianagaram, Andhra Pradesh from January 2020 to June 2021.

Study Design: Randomized controlled, double-blind study.

Study Location: This study was done at a tertiary care teaching hospital-based study in the Department of Anesthesia, at Maharaja Institute of medical sciences, Vizianagaram, Andhra Pradesh, India.

Study Duration: January 2020 to June 2021

Sample size: 60 patients.

Sample size calculation: As per the study done by **Srivatsava et al**.[13], considering a 30% reduction in the requirement of additional sedation needs, the sample size is calculated with 80% power at a confidence level of 95%, the sample size came to be 32 in each group. As the data is incomplete for 2 patients, 30 patients were included in each group.

Subjects & selection method: Patients posted for lower limb and lower abdominal surgeries at Maharaja Institute of medical sciences during the study duration were selected.

Group C: 30 Patients: Received 15 ml of 0.75% of Ropivacaine with 1 mcg/kg of Clonidine epidurally.

Group D: 30 Patients: Received 15ml of 0.75% of Ropivacaine with 1 mcg/kg of Dexmedetomidine epidurally.

Inclusion criteria:

1. Patients belonging to ASA grades I and II
2. Either sex
3. Aged 18-65 years,
4. Patients undergoing lower limb and abdominal surgeries under CSEA.
5. Patients who provided informed consent

Exclusion criteria:

1. Pregnant and lactating women;
2. Patients undergoing emergency surgeries and cesarean sections
3. Patients with a history of drug or alcohol abuse.
4. Patients with known allergies to clonidine or dexmedetomidine
5. Patients with contraindications to spinal and epidural anaesthesia-elevated intracranial pressure, intracranial mass or infection at the site of procedure etc.

Procedure methodology

After getting written informed consent was obtained, this study was conducted. Patients were kept nil by mouth for 8 hours before surgery.All patients were operated under Combined Spinal Epidural anesthesia.Baseline heart rate, blood pressure, and respiratory rate monitored. With an 18G cannula IV line was secured and infusion was started.

The patient was kept in left lateral flexed position. Ensuring aseptic conditions18G TOUHY needle was used to identify the epidural space. Through the epidural needle 18G PORTEX, epidural catheter was passed till 2-3cm of the catheter is in the space. Catheter fixed to the back is withdrawn. As a test dose, 3cc of 2% lignocaine with adrenaline 1:2,00,000 was injected through the catheter and observed for any intravascular or intrathecal injection. The epidural catheter was fixed. In lower space to the epidural, 23G or 25G Quincke's Spinal needle was introduced. Lumbar Puncture was done. Inj 0.75% Ropivacaine 2.5 – 3 ml was injected. Level of sensory blockade was noted. There was no administration of narcotics throughout the intra-operative period. Patients were sedated intraoperativelyusing Midazolam (0.05-0.15mg/kg).

Fluid management: Standard fluids were given intraoperatively as per the patient's weight. After surgery, patients were shifted to the ward and monitored. VAS score was used to monitor pain.

"0" on VAS → no pain

"10" on VAS → worst possible pain.

Readings of >5 was considered as unsatisfactory analgesia and rescue analgesia was given. The time interval between start of analgesia (that is when VAS score is at 5), till the patient's complaint of pain (that is when VAS score is >5) when the rescue analgesia was given is called as duration of analgesia. The time at which rescue analgesia was given, was noted.

Ethical considerations: Permission was obtained from the Institutional ethical committee attached to Maharaja Institute of Medical Sciences, Vizianagaram before conducting the study. Every patient was explained the whole process and advantages of the study. After he/she accepts, an informed consent form is given in local language or the patient understandable language and the person was asked to sign it or put a thumb impression.

Statistical analysis:

Statistical analysis was done using Epi info software version 7.2.5. Student's *t*-test was used to compare numerical parameters between two groups. Chi square test was used to compare categorical parameters between two groups. P value <0.05 was considered significant.

III. Results

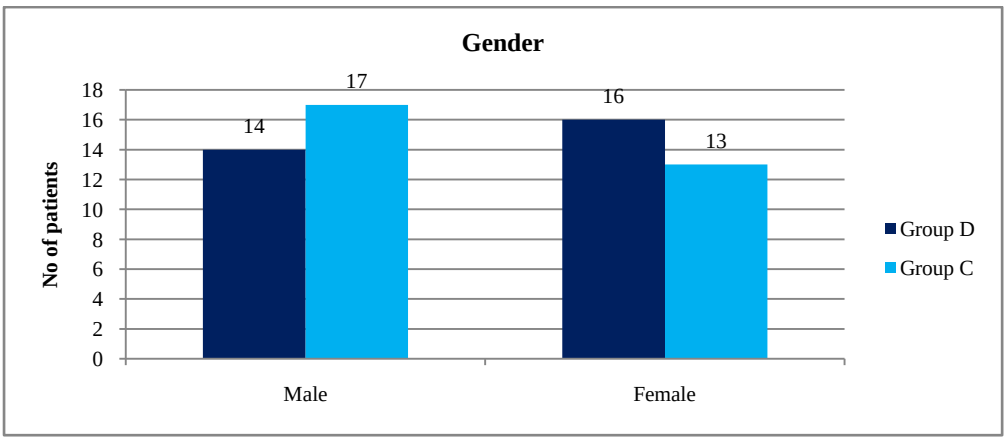
Sixty adult patients aged between 18-65 years of class ASA-PS I and ASA-PS II of either sex of the Vizianagaram population, scheduled for elective lower abdominal surgeries and lower extremity surgeries were selected for the study. **Table 1** shows the age distribution

Age (Years)	Group D (n=30) Ropivacaine + Dexmedetomidine		Group C (n=30) Ropivacaine + Clonidine	
	No. of cases	% of cases	No. of cases	% of cases
18-30	7	23.3	9	30.0
31-40	9	30.0	7	23.3
41-50	10	33.3	8	26.7
51-65	4	13.3	6	20.0
Total	**30**	**100**	**30**	**100**

Table 1 shows that more than 60 % of patients belonged to the age 31 to 50 years of age in Group D, whereas, in Group C, patients are equally distributed in all the age groups. The average age of the patient in group D was 40.03 ± 10.70 years, and in group C was 40.40 ± 11.94 years. There is no significant difference in the mean age of patients of the two groups(p=0.899).Age incidences between the 2 groups were comparable.

Gender: There were 17 males in group C and 14 males in group D. There were 16 females in group D and 13 females in group C.

Graph 1 shows gender distribution in both groups.



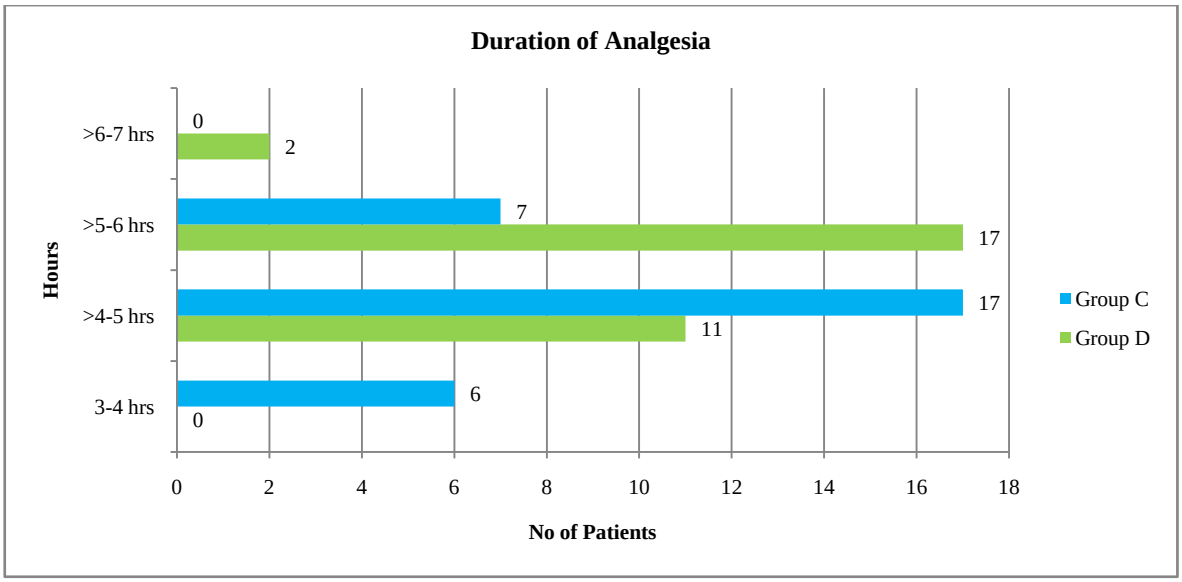
Time of onset of analgesia: The mean time for onset of analgesia in group-D was 10.8±1.854 minutes, and in group-C, it was11.96 ± 1.99 minutes. 43.3% of patients in group-D had an onset between 5-10 minutes followed by 56.6% patients had onset in between 11-15 minutes, and about 33.3% of patients in group-C had an onset between 6-10 minutes followed by 60% of patients had onset in between 11-15 minutes and 6.67% patients had onset in between 16-20minutes. There is significant difference in the time of onset of analgesia between groups. (P = 0.01). It was quick in group D patients.

Table 2 shows the time of onset of analgesia

ONSET OF ANALGESIA (mins)	Group I		Group II	
	No. of cases	(%)	No. of cases	(%)
1-5	0	0.0	0	0.0
6-10	13	43.3	10	33.3
11-15	17	56.6	18	60.0
16-20	0	0.0	2	6.67

Duration of analgesia: Duration of analgesia in group C ranged from 3-6 hours with a mean duration of 275.66±38.16 minutes. More than 50% of group C patients had a duration of analgesia between 4-5 hours. Duration of analgesia in group-D ranged from 3-7 hours with a mean duration of 297.33±35.91 minutes. 50% of patients in group-D had a duration of analgesia between 5-6 hours. Duration of analgesia was significantly more in group D compared to group C. (P<0.001).

Graph 2 shows duration of analgesia.



Quality of analgesia assessed at time of giving rescue analgesia to the patient: The patient was asked to give a global assessment of overall effectiveness of analgesic treatment. In group C, 43.3% of patients had a pain score of 3 than group-I of patients (36.7%). In group-D, 60% of patients had a pain score of 4, whereas, in group C, 50% had a pain score 4. This difference was statistically insignificant by the chi-square test. (X^2 = 0.42, df=1, P> 0.05)

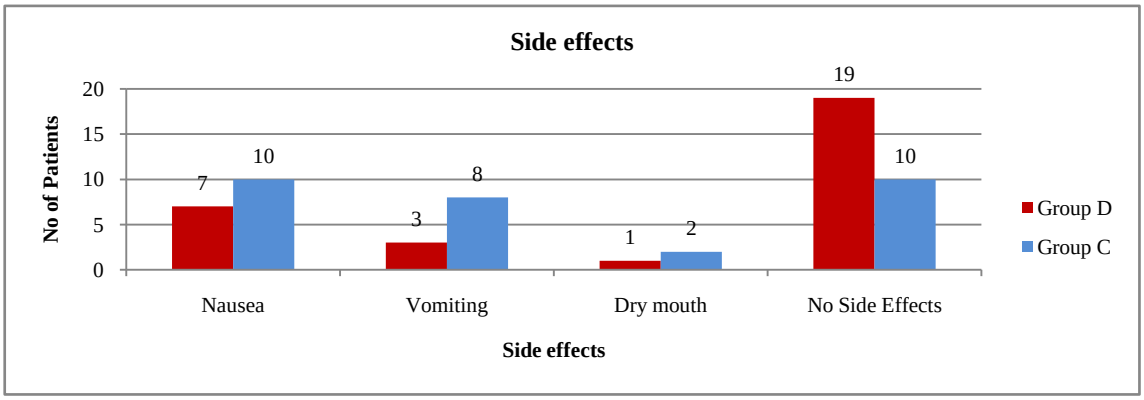
Table 3: Shows the quality of analgesia in both groups

Quality of Analgesia	Group D		Group C	
	Cases	(%)	Cases	(%)
No Pain Relief	0	0.0	0	0.0
Poor Pain Relief	0	0.0	0	0.0
Fair Pain Relief	1	3.3	2	6.7
Good Pain Relief	11	36.7	13	43.3
Excellent Pain Relief	18	60.0	15	50.0
Total	30	100	30	100

Hemodynamic changes: There was a significant fall in heart rate by 20% between 30 to 50 minutes of epidural
injection in two groups; but there was no significant difference in reduction of heart rate between the two groups. (p=0.592) There was a significant fall in the mean arterial pressure by 25% between 40 to 50 minutes in two groups, but there was no significant difference in incidence of hypotension between the two groups. (p=0.796)

Side Effects: In group-D, nausea (23.3%), vomiting (10%) & dry mouth (1%) were less than group-C, in which nausea was seen among 33.34% of patients, vomiting was seen in 26.67% of patients, dry mouth was seen in 6.67% of patients. These differences were statistically significant by the chi-square test. (P < 0.05).

Graph 3 shows side effects in both groups



IV. Discussion

In the current study we compared the efficacy and safety of epidural adjuvants named dexmedetomidine and clonidine among patients scheduled for lower limb and lower abdominal surgeries.

Several studies have used epidural clonidine in the doses of 1-4mcg/kg, and observed hemodynamic side effects as dose-dependent. Epidural clonidine at a dose 1mcg/kg prolongs analgesia without producing unwanted side effects. Epidural Dexmedetomidine was studies at doses ranging from 1-2mcg/kg and at doses less than 1mcg/kg.

There was no statistically significant difference(p>0.05) in age and gender between groups.

Our study showed a significantly earlier sensory blockade onset among patients receiving Dexmedetomidine compared to patients receiving Clonidine. Onset of analgesia is quick and duration is more significantly in D group compared to C group patients.Bajwa et al[14] found the analgesic onset at T10 was faster in Dexmedetomidine group (8.52±2.36min) Compared to Clonidine (9.72±3.44min). When Dexmedetomidine is administrated epidurally it reaches a maximum concentration in the CSF within 5 minutes with a distribution half-life of 0.7 minutes. There is a dose-dependent antinociceptive effect of epidural dexmedetomidine which has been associated with its affinity for the alpha 2 receptors on the spinal cord.

Saravana Babu *et al.*[15] concluded that epidural route provides acceptable postoperative analgesia. Dexmedetomidine is a better adjunct to ropivacaine in comparison to clonidine in terms of onset and postoperative analgesia and stable cardiorespiratory parameters. This study is in complete agreement with our study findings.

The study done by Bajwa, found a significantly longer duration for 1st rescue top-up in the Dexmedetomidine group compared to the clonidine group. This could bedue tothe onset of incisional pain to indicate analgesia time, But, higher doses of Dexmedetomidine (1.5mcg/kg) and Clonidine (2mcg/kg) may be considered to explain the prolonged duration in comparison to our study.

Neogi et al. [16]studied the characteristics of Clonidine (1mcg/kg) & Dexmedetomidine (1mcg/kg) with 0.25% Ropivacaine when given caudal analgesia postoperatively in children & found that the mean duration was not significantly prolonged between the groups receiving Clonidine and Dexmedetomidine.

In our study, heart rate significantly fell in both groups by 20 in 30 to 50 minutes after the epidural injection. Blood pressure decreased by 25% in 30 to 50 minutes following epidural injection.

Gudul Z et al.[17]noticed significantreduction in the mean blood pressure with ropivacaine compared to bupivacaine at 10 min and 20 min after the blockade.Heart rate significantly fell in both groups by 20 in 30 to 50 minutes after the epidural injection. Blood pressure decreased by 25% in 30 to 50 minutes following epidural injection.We observed similar hemodynamic changes in both groups with no significant difference. Nausea was

seen in ten patients in group C and seven patients in group D. Vomiting was observed in eight patients in group C and three patients in group D. We had two patients in group C and one patient in group D who had a dry mouth. Shivering was not observed in two groups.

Bajwa et al[14]showed increased incidence of nausea, dry mouth in his study.We also identified some cases of nausea and dry mouth.

Chandran *et al*.[18] compared the effectiveness of ropivacaine 0.75% and 0.5% bupivacaine and concluded that ropivacaine and bupivacaine produced equally effective anesthesia. 0.75% ropivacaine produced adequate intensity of motor and sensory blockades and is comparable with 0.5% bupivacaine. Hence, we used 0.75% ropivacaine to provide epidural anaesthesia in our study in both groups.

Larger studies with more sample size, using different concentrations of both drugs are recommended in future.

V. Conclusion

We conclude that the addition of 1mcg/kg Dexmedetomidine as an adjuvant to 0.75% Ropivacaine in epidural anesthesia causes an early onset and prolonged duration of sensory analgesia in comparison to 1mcg/kg Clonidine. Epidural dexmedetomidine causes better sedation as compared to Clonidine.

The study is self- sponsored.

There were no conflicts of interest.

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