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Research Article

TO COMPARE DEXMEDETOMIDINE WITH CLONIDINE AS ADJUVANTS TO ROPIVACAINE IN EPIDURAL ANESTHESIA IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERIES

TAMILISETTI VIDYA SAGAR[1], YATISH BYNDOOR[2], MADHAV P[2]

[1]Department of Pharmacology, GSL Medical College, Rajahmundry, Andhra Pradesh, India. [2]Department of Pharmacology, Apollo Institute of Medical Sciences and Research, Chittoor, Andhra Pradesh, India. Email: Dr.yati1988@gmail.com

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ABSTRACT

Objective: The objective of the study is to compare dexmedetomidine with clonidine as adjuvants to ropivacaine in epidural anesthesia in the onset of sensory and motor blockade, duration of post-operative analgesia, level of sedation, and occurrence of side effects.

Methods: This study was a prospective randomized observational and comparative study. Sixty patients of age between 20 and 50 years with the American Society of Anesthesiologists grade I and II physical status belonging to both sexes undergoing abdominal surgeries under epidural anesthesia are included; patients were allocated randomly into two groups comprising 30 patients in each group. Group A patients are given injection dexmedetomidine, added to ropivacaine and Group B patients are given injection clonidine, added to ropivacaine by epidural route. Following parameters were observed intra and post-operatively: Onset of sensory and motor blockade and duration of motor blockade, level of sedation, duration of analgesia, and side effects. All data are presented in tabular form as mean ± standard deviation. The analysis is done by unpaired *t*-test. Statistical analysis is done using SPSS software.

Results: Mean time of onset of sensory blockade in Group A was 9.50 min with standard deviation of 1.85 and in Group B was 9.48 min with standard deviation of 1.60. Mean time of onset of motor blockade in Group A was 20.66 min with standard deviation of 2.83 and in Group B was 20.48 min with standard deviation of 2.52. Mean duration of analgesia in Group A was 312.66 min with standard deviation of 22.02 and in Group B was 314.20 min with standard deviation of 24.58. There is no statistical difference between two groups in the level of sedation which was assessed by Wilson's sedation scale. Side effects most commonly observed are hypotension and bradycardia.

Conclusion: We conclude that both dexmedetomidine and clonidine are similar in efficacy and tolerability as adjuvants in the onset of sensory and motor blockade and post-operative analgesia when added to ropivacaine in epidural anesthesia.

Keywords: Dexmedetomidine, Clonidine, Ropivacaine, Epidural anesthesia and Bromage scale.

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INTRODUCTION

Epidural anesthesia is a technique for perioperative pain management with multiple applications in anesthesiology. It can be single shot or continuous infusion for long-term pain relief. Aside from benefit of potentially providing excellent analgesia, its use reduces exposure to other anesthetics and analgesics, decreasing side effects [1-3]. It has also shown to decrease cortisol levels, expedite return of bowel function, decrease incidence of pulmonary embolism and deep venous thrombosis in post-operative period, and shorten lengths of in-hospital stay [4,5].

Ropivacaine is new, long-acting local anesthetic, first synthesized by Ekenstam *et al*. [6]. It is first pure S-enantiomer and in comparison to bupivacaine has similar analgesic properties, lesser motor blockade, and decreased propensity of cardiotoxicity [7].

Local anesthetics do have potential to produce deleterious effects such as cardiac arrhythmias, central nervous system (CNS) depression, seizures, respiratory depression, hypertension, and allergic reactions [8].

Adjuvants limit cumulative dose requirement of local anesthetic and has potential to improve efficacy and decrease local anesthetic toxicity. Several techniques, drug regimens, and additives such as opioids and alpha-2 adrenoreceptor agonists have been used to improve quality of block and prolong duration and intensity of blockade [9,10].

Alpha 2 adrenergic agonists have both analgesic and sedative properties when used as adjuvants to local anesthesia. They act at spinal and supraspinal levels of CNS [11]. Clonidine and dexmedetomidine are alpha-2 adrenergic agonists, which have analgesic properties and potentiate local anesthetic effects [12-14].

Clonidine, selective alpha-2 adrenergic agonist, prolong duration of sensory and motor blockade, and reduce amount of local anesthetic required to produce post-operative analgesia [15], effectively used as adjuvant to spinal anesthesia in many studies [16]. It has also been shown to have peripheral analgesic action after administration by epidural, intravenous route, wound infiltration, and topical application in various clinical studies [17].

Dexmedetomidine, another selective alpha-2 adrenergic agonist with alpha-2/alpha-1 selectivity ratio 8–10 times higher than clonidine, has been shown to prolong duration of block and post-operative analgesia when added to local anesthetic in various regional blocks [18-20].

In our country, limited number of studies compared dexmedetomidine with clonidine as adjuvants to local anesthesia, our study aimed to compare effect of clonidine and dexmedetomidine when given as adjuvant to ropivacaine in epidural anesthesia.

METHODS

This was a prospective randomized, open-labeled, observational and comparative study carried out in department of anesthesiology. The study was approved by institutional ethical committee. A total number of 60 patients were included and were allocated randomly into two groups comprising 30 patients in each group. Group A consists of patients whom injection clonidine is added to ropivacaine administered epidurally.

Group B consists of patients whom injection dexmedetomidine is added to ropivacaine and administered epidurally. Study medications as per method were coded and given by an anesthetist during surgery period. At end of the study, code of two drugs was open for analysis.

Patients of age between 20 and 50 years with the American Society of Anesthesiologists (ASA) grade I and II physical status belonging to both sexes undergoing abdominal surgeries under epidural anesthesia are included in study. Patients with ASA Grade ≥III and contraindications to regional anesthetics are excluded, informed written consent was obtained from all 60 patients after detailed explanation of procedure before enrollment, during pre-operative visit patient's detailed history, physical and systemic examination were carried out.

All patients were pre-medicated with injection midazolam 0.05 mg/kg I.M 45–60 min before procedure, peripheral venous cannulation was done with18/16 G IV cannula, and all patients were pre-loaded with 10 mL/kg of Lactated Ringer's solution. Patients were placed in left lateral position, after local infiltration with 1% lignocaine, epidural space was identified with Tuohy needle at L2-L3/L3-L4 interspace based on height of individual by loss of resistance technique. 18G epidural catheter was threaded through a needle into epidural space for 3–4 cm and secured with adhesive tapes. After negative aspiration for blood and cerebrospinal fluid, 3 mL of 2% lignocaine with 15 μg of adrenaline was given as test dose was given and patient was turned to supine position. After 5 min, if there is no adverse reaction to test dose, intravascular and intrathecal placement were ruled out and study drugs were administered.

Group A patients are given injection dexmedetomidine 1.5 μg/kg (made to 1 mL) added to 19 mL of 0.75% ropivacaine by epidural route. Group B patients are given injection clonidine 2 μg/kg (made to 1 mL) added to 19 mL of 0.75% ropivacaine by epidural route. In both groups, time of injection was recorded as zero hours, and following parameters were observed intraoperatively and post-operatively: Onset of sensory blockade, onset, and duration of motor blockade which is taken as time from injection to return of power to Bromage Grade 0, degree of sedation, duration of analgesia, and side effects. Bilateral pin-prick method was used to evaluate and check sensory levels. Modified Bromage scale was used to measure motor blockade effect. Grading of sedation was evaluated by Wilson's sedation scale.

Table 1: Modified Bromage Scale [21]

Grade	Criteria	Degree of block (%)
0	Free movement of legs and feet raise extended leg	Nil (0)
1	Just able to flex knees with free movement of feet flexion is decreased but a full extension of feet and ankles is present	Partial (33)
2	Unable to flex knees with free movement of feet ankle and feet present	Partial (66)
3	Unable to move legs or feet move toes	Complete paralysis (100)

Table 2: Wilson sedation score [22]

Score	Signs
1	Fully awake and oriented
2	Drowsy
3	Eyes closed but responsive to command
4	Eyes closed but responsive to mild physical stimulation
5	Eyes closed but unresponsive to mild physical stimulation

Cardiorespiratory parameters were monitored continuously till the end of procedure, and recordings were noted. Hypotension was treated with injection mephentermine and heart rate <50 beats/min was treated with injection atropine. Intravenous fluids were given as per body weight and operative loss requirement. If respiratory rate was <10/min, respiratory depression was diagnosed. Side effects such as nausea, vomiting, bradycardia and hypotension, respiratory depression, dry mouth, and shivering were noted in both groups.

At end of surgery, patient was shifted to post-operative ward. All vital and hemodynamic parameters were recorded at regular intervals. A post-operatively visual analog scale score was noted. Duration of analgesia was calculated when visual analog scale reached 4 or more or when patient demanded rescue analgesia, pain was managed with top-up of 10 mL of 0.2% ropivacaine post-operatively.

At end of study, all data are compiled and presented in tabular form as mean ± standard deviation. Two study groups were compared using unpaired t-test. Statistical analysis is done using the Statistical Package for the Social Science version 17 for windows.

RESULTS

Results were analyzed in both groups based on various parameters such as age, gender, weight, height, onset of sensory and motor blockade, duration of motor blockade, duration of analgesia, sedation score, hemodynamic parameters, and occurrence of side effects.

DISCUSSION

In our study, we used low concentrations of clonidine and dexmedetomidine as adjuvants to ropivacaine as there are no studies

Table 3: Age distribution in each group

Age (years)	Group A	Group B
20–30	9	9
31–40	14	12
41–50	7	9
Mean±SD	36±2.74	34.9±2.2

SD: Standard deviation

Table 4: Gender distribution in each group

Sex	Group A	Group B
Male	13	14
Female	17	16
Total	30	30

Table 5: Weight distribution in each group

Weight (kg)	Group A	Group B
Range	46–70	46–70
Mean±SD	57.93±6.20	57.72±6.29

SD: Standard deviation

Table 6: The height distribution in each group

Height (cm)	Group A	Group B
Range	150–170	150–170
Mean±SD	155.3±5.79	155.26±5.96

SD: Standard deviation

Table 7: Mean time of onset of sensory blockade in each group

Group	Mean±SD
A	9.50±1.85
B	9.48±1.60
P	>0.05

SD: Standard deviation

Table 8: Mean time of onset of the motor blockade in each group

Group	Mean±SD
A	20.66±2.83
B	20.48±2.52
P	>0.05

SD: Standard deviation

Table 9: Duration of the motor blockade in each group

Group	Mean±SD
A	233.33±27.92
B	232.66±27.56
P	>0.05

SD: Standard deviation

Table 10: Duration of analgesia in each group

Group	Mean±SD
A	312.66±22.02
B	314.20±24.58
P	>0.05

SD: Standard deviation

documenting equivalent doses of epidural dexmedetomidine and clonidine [23-25].

Mean time of onset of sensory blockade to T10 level in Group A was 9.50 min with standard deviation of 1.85 and in Group B was 9.48 min with standard deviation of 1.60. Statistical analysis by unpaired t-test shows no significant difference. This is in contrast with study of Bajwa *et al*. [13] who found that onset of sensory blockade at T10 was faster in group receiving dexmedetomidine when compared to patients receiving clonidine.

Mean time of onset of onset of motor blockade in Group A was 20.66 min with standard deviation of 2.83 and in Group B was 20.48 min with standard deviation of 2.52 and there is no significant difference between two groups. This is in contrast with study of Bajwa *et al*. [13] who found that patients receiving dexmedetomidine achieved grade 3 motor blockades in less time than those receiving clonidine.

Mean duration of the motor blockade in Group A was 233.33 min with standard deviation of 27.92 and in Group B was 232.66 min with standard deviation of 27.56 and there is no significant difference between two groups. Studies done by Kanazi *et al.* [26] and Al Ghanem *et al.* [27] concluded that dexmedetomidine and clonidine added to bupivacaine produced similar prolongation in duration of motor and sensory block; these studies are in agreement with our study.

There is no significant statistical difference in level of sedation between two groups in contrast to study conducted by Oriol-Lopez *et al*. [28] which showed higher level of sedation with dexmedetomidine when compared to clonidine.

Mean duration of analgesia in Group A was 312.66 min with standard deviation of 22.02 and in Group B was 314.20 min with standard deviation of 24.58 and there is no significant difference between two groups but there is significant prolongation of duration of analgesia. This is in contrast with study done by Neogi *et al*. [29] who found that mean duration of analgesia was not significantly prolonged between two groups receiving clonidine and dexmedetomidine. Studies conducted by Reddy *et al.* [9] and Harsoor *et al.* [10] showed significant prolongation of duration of analgesia, results which are similar to our study.

Side effects observed in both groups are hypotension and bradycardia; these results were similar to study done by Swami *et al*. [14]. There is

Table 11: Mean±standard deviation of pulse rate, systolic blood pressure, and diastolic blood pressure of each group

Group	Mean±SD		
	Pulse rate	SBP	DBP
A	75.8±4.56	105.42±8.29	72.28±4.55
B	74.04±4.77	106.34±8.24	74.68±5.31
P	>0.05	>0.05	>0.05

SD: Standard deviation, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 12: Sedation scores in each group

Sedation score	Group A	Group B
1	15	14
2	6	8
3	9	8
4	0	0
5	0	0

Table 13: Occurrence of side effects in each group

Side effects	Group A	Group B
Hypotension	3	3
Bradycardia	8	8
Nausea	4	4
Vomiting	0	0
Shivering	0	0
Dry mouth	5	5
Respiratory depression	0	0

no difference in hemodynamic response parameters during and after anesthesia in between two study groups. These results were similar to study done by Kumar *et al.* [30]. A study done by Tripathi *et al.* [31] found that clonidine is safe and effective in preventing hemodynamic stress response during laparoscopic cholecystectomy.

Agarwal *et al.* [11] compared dexmedetomidine and clonidine and found that patients who received either of two drugs required lower doses of rescue analgesic agents in post-operative period. These results were similar to our study.

None of the patients required sedation intraoperative and they were comfortable throughout surgery with arousable sedative effects. This can be explained on the basis that some amount of systemic absorption of drug could be present [32].

Respiratory depression, a feared side effect is not seen in any of the patient, Belleville *et al.* reported episodes of obstructive apnea in a group of patients who received high doses of dexmedetomidine [33].

Nausea, vomiting, and dry mouth were observed in patients of either group equally. This is in contrast to study done by Eren *et al.* [34] which showed higher incidence of dry mouth during post-operative period with dexmedetomidine.

CONCLUSION

We conclude that dexmedetomidine can be useful adjuvant during local anesthesia and can be an alternative to clonidine in terms of onset of sensory and motor blockade, sedation, hemodynamic stability, and duration of post-operative analgesia with minimal and transient side effects.

Limitations

Possible limitations are unable to identify ideal scale for assessment of quality of block achieved, low dose of drugs used, small sample size,

and inability to monitor serum concentration of drugs, onset of pain at surgical incisional site may not give accurate duration of analgesia, as different surgeries have been taken into the study, further studies are needed to determine cost-effectiveness.

AUTHORS CONTRIBUTION

Research material and data analysis were done by Dr. Sagar, and Statistical analysis and proofreading by Dr. Yatish Byndoor.

CONFLICTS OF INTERESTS

Nil.

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