Assessment of epidural clonidine as an adjuvant to local anesthetic in lower abdominal and lower limb surgeries

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ABSTRACT

Background: Continuous epidural techniques and recent improvements in spinal catheters make the epidural and intrathecal spaces easily accessible for repetitive administration of local anesthetics to extend anesthesia. The present study was conducted to assess epidural clonidine as an adjuvant to local anesthetic in lower abdominal and lower limb surgeries.

Materials & Methods: 70 patients scheduled for elective lower abdominal, gynaecological and lower limb surgeries under epidural anesthesia of both genders were divided into 2 groups of 35 each. In group I, 0.5% bupivacaine + 0.9% normal saline, 1 ml was used and in group II, 0.5% bupivacaine + Inj. Clonidine 2μg/kg (1 ml) was used. Parameters such as height, weight, mean arterial pressure, pulse rate, duration of motor blockade, duration of analgesia (in minutes), sedation score and side effects were recorded.

Results: Group I had 18 males and 17 females and group II had 20 males and 15 females. The mean weight was 54.7 kgs and 54.2 kgs, height was 165.2 cm and 164.9 cm, mean arterial pressure (mm Hg) was 86.2 and 76.1, mean pulse rate (beats/min) was 73.2 and 62.5, duration of motor blockade (in minutes) was 104.2 and 312.8, duration of analgesia (in minutes) was 140.2 and 376.4 in group I and II respectively. The difference was significant (P< 0.05). Score 1 was seen in 20 in group I, score 2 in 15 in group I and 8 in group II, score 3 in 14 in group II, score 4 in 7 in group II and score 5 in 6 in group II. The difference was significant (P< 0.05). Shivering was seen in 4 in group I, nausea in 2 in group I and vomiting 3 in group I and 1 in group II. The difference was significant (P< 0.05).

Conclusion: There was an increase in the duration of analgesia following the addition of clonidine to bupivacaine 2 ug/kg in comparison to bupivacaine alone when instilled in the epidural space.

Key words: bupivacaine, clonidine, analgesia

Introduction

Continuous epidural techniques and recent improvements in spinal catheters make the epidural and intrathecal spaces easily accessible for repetitive administration of local anesthetics to extend anesthesia.[1,2] Attenuation of postoperative pain, especially with certain types of analgesic regimens, may decrease perioperative morbidity and mortality. Acute pain results in potentially life-threatening problems.[3] Epidural anesthesia with local anesthetics, reduces physiologic responses to surgery and also provides superior pain relief. Various adjuvants like opioids, epinephrine, clonidine, ketamine, neostigmine, adenosine, midazolam, magnesium, verapamil, ketorolac, etc. have been tried with local anesthetics in the epidural space, to enhance analgesia while minimizing side effects.[4]

Clonidine, an alpha-adrenergic agonist, prolongs the duration of action of local anesthetics after intrathecal or epidural injection. This effect may result from local vasoconstriction and local altered local anesthetic disposition, or from a direct analgesic effect on alpha-adrenoceptors in the substantia gelatinosa of the spinal cord.[5] The analgesic effect of clonidine is more potent after neuraxial administration which points to a spinal site of action, thus favouring neuraxial (intrathecal or epidural) administration.[6] Epidural or intrathecal administration of clonidine potentiates the anesthetic action and reduces the dose requirement of volatile or injectable general or regional anesthetic agents with correspondingly fewer side effects.[7,8] The present study was conducted to assess epidural clonidine as an adjuvant to local anesthetic in lower abdominal and lower limb surgeries.

Materials & Methods

The present study consisted of 70 patients scheduled for elective lower abdominal, gynaecological and lower limb surgeries under epidural anesthesia of both genders. All gave their written consent to participate in the study.

Data such as name, age, gender etc. was recorded. Patients were divided into 2 groups of 35 each. In group I, 0.5% bupivacaine + 0.9% normal saline, 1 ml was used and in group II, 0.5% bupivacaine + Inj. Clonidine 2μg/kg (1 ml) was used. Parameters such as height, weight, mean arterial pressure, pulse rate, duration of motor blockade, duration of analgesia (in minutes), sedation score and side effects were recorded. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I Distribution of patients

Groups	Group I	Group II
Agent	0.5% bupivacaine + 0.9% normal saline	0.5% bupivacaine + Inj. Clonidine 2µg/kg
M:F	18:17	20:15

Table I shows that group I had 18 males and 17 females and group II had 20 males and 15 females.

Table II Assessment of parameters

Parameters	Group I	Group II	P value
Weight (in Kg)	54.7	54.2	0.91
Height (in cm)	165.2	164.9	0.83
Mean arterial pressure (mm Hg)	86.2	76.1	0.01
Mean pulse rate (beats/min)	73.2	62.5	0.02
duration of motor blockade	104.2	312.8	0.001
duration of analgesia (in minutes)	140.2	376.4	0.001

Table II shows that mean weight was 54.7 kgs and 54.2 kgs, height was 165.2 cm and 164.9 cm, mean arterial pressure (mm Hg) was 86.2 and 76.1, mean pulse rate (beats/min) was 73.2 and 62.5, duration of motor blockade (in minutes) was 104.2 and 312.8, duration of analgesia (in minutes) was 140.2 and 376.4 in group I and II respectively. The difference was significant (P< 0.05).

Table III Comparison of sedation score

Parameters	Group I	Group II	P value
Score 1	20	0	0.01
Score 2	15	8	
Score 3	0	14	
Score 4	0	7	
Score 5	0	6	

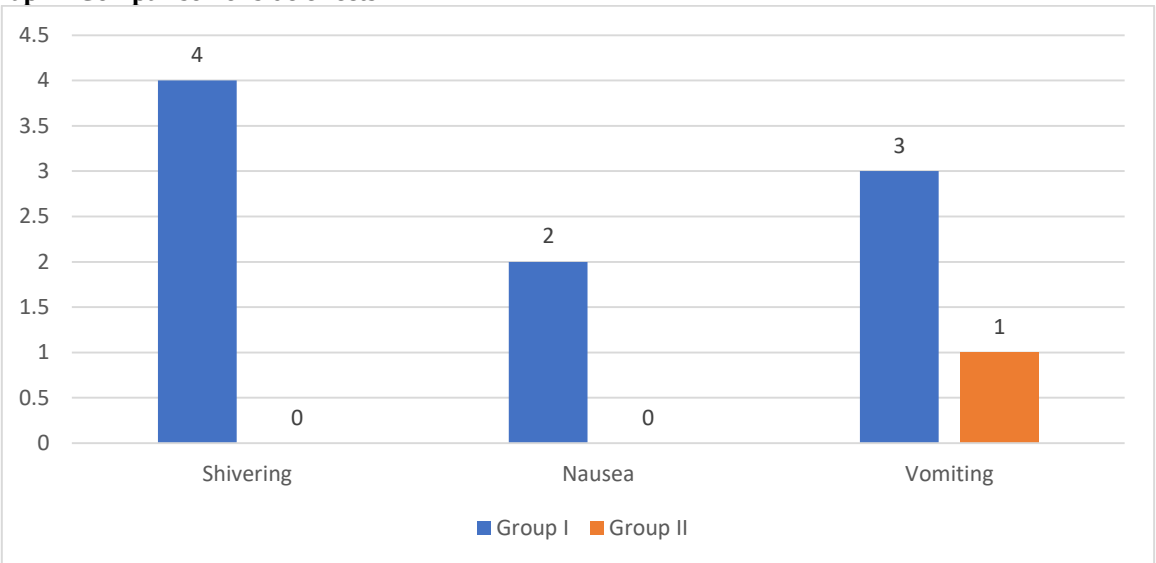
Table III shows that score 1 was seen in 20 in group I, score 2 in 15 in group I and 8 in group II, score 3 in 14 in group II, score 4 in 7 in group II and score 5 in 6 in group II. The difference was significant (P< 0.05).

Table IV Comparison of side effects

Side effects	Group I	Group II	P value
Shivering	4	0	0.01
Nausea	2	0	
Vomiting	3	1	

Table IV, graph I shows that shivering was seen in 4 in group I, nausea in 2 in group I and vomiting 3 in group I and 1 in group II. The difference was significant (P< 0.05).

Graph I Comparison of side effects



Discussion

Clonidine being a partial α2 adrenergic agonist has antihypertensive effects and can potentiate effects of local anesthetics.[9,10] It acts by opioids-independent mechanism, stimulates α2 adrenoreceptors reducing central neural transmission in spinal neurons, and inhibits the release of substance-P.[11] It acts pre-synaptically interfering with nitric oxide mechanisms and protein kinases as well as by stimulation of cholinergic interneuron. Anaesthesia was prolonged when clonidine was added to local anaesthetics for peripheral nerve blocks.[12,13] The present study was conducted to assess epidural clonidine as an adjuvant to local anesthetic in lower abdominal and lower limb surgeries.

We found that group I had 18 males and 17 females and group II had 20 males and 15 females. Arora et al[14] compared the onset and duration of sensory anesthesia, motor paralysis and duration of analgesia using 0.5% plain bupivacaine, with clonidine (2μg/kg) in patients posted for lower abdominal and lower limb surgeries under epidural anaesthesia. 62 Patients posted for elective lower abdominal, gynaecological and lower limb surgeries under epidural anesthesia, aged 18 to 60 years, height more than 150 cms of ASA physical status 1 or 2 were included. All patients were randomized into two groups of 31 individuals each. Clonidine in the dose of 2μg/kg added to bupivacaine injected into epidural space significantly prolonged the duration of analgesia when compared to bupivacaine alone. No effect on the onset of sensory and motor blockade was observed. However, it increases the duration of motor blockade. Clonidine also has effect on sedation level, pulse rate and mean arterial blood pressure.

We found that the mean weight was 54.7 kgs and 54.2 kgs, height was 165.2 cm and 164.9 cm, mean arterial pressure (mm Hg) was 86.2 and 76.1, mean pulse rate (beats/min) was 73.2 and 62.5, duration of motor blockade (in minutes) was 104.2 and 312.8, duration of analgesia (in minutes) was 140.2 and 376.4 in group I and II respectively. Klimscha et al[15] compared hemodynamic and analgesic effects of spinal versus epidural clonidine alone and after repetitive dosing. They evaluated 40 patients scheduled for lower extremity orthopedic surgery under continuous spinal or epidural anesthesia with bupivacaine 0.5% (initial dose 5 mg and 50 mg, respectively). In either spinal or epidural technique one-half of patients received clonidine (150 micrograms) in addition to bupivacaine. Repeat doses of the same anesthetic mixture were allowed in cases of subsequent pain. Mean arterial pressure (MAP) and heart rate were recorded for 6 h after each injection. Duration of clinically useful anesthesia was defined as the time from drug administration to first sensation of pain. Intrathecal, but not epidural, clonidine decreased MAP significantly compared with bupivacaine alone. MAP after intrathecal clonidine with bupivacaine was lower than epidural clonidine with bupivacaine 5 and 6 h after injection. Repetitive administration caused no further decrease in MAP. Onset time required to surgical anesthesia (sensory block of T11) did not differ among the four groups. Duration of spinal and epidural anesthesia was increased more than two folds by clonidine.

We observed that score 1 was seen in 20 in group I, score 2 in 15 in group I and 8 in group II, score 3 in 14 in group II, score 4 in 7 in group II and score 5 in 6 in group II. Shivering was seen in 4 in group I, nausea in 2 in group I and vomiting 3 in group I and 1 in group II. Fakuda et al[16] in their study clonidine was combined with local anesthetics. Intrathecal and epidural injection of local anesthetic decrease MAP and sympathetic outflow, presumably by blocking axonal transmission along spinal roots and nerves. Therefore, one would expect the spinal preganglionic sympathetic cellular inhibition by clonidine would be hidden by dense nxonal blockade by local anesthetic, thus explaining why intrathecal clonidine does not decrease blood pressure more with a large dose (15 mg) of bupivacaine (2), than with a small dose. Although it is tempting to speculate that decrease in MAP after intrathecal, but not epidural, clonidine observed in this study reflects more profound sympatholysis in the spinal cord, the density of axonal block from 50 mg epidural bupivacaine probably was greater than that of 5 mg spinal bupivacaine, as evidenced by a greater decrease in MAP by bupivacaine alone.

Giovanni Cucchiaro[17] compared the incidence of vomiting and pruritus as well as the analgesic profile and sedation score of three different combinations of bupivacaine, fentanyl, and clonidine administered epidurally in patients undergoing Nuss procedure. They found no significant difference in the sedation score. They found that the number of patients who experienced vomiting was significantly less in the clonidine group. The number of patients who experienced pruritus was significantly less in the clonidine group versus the other groups. Huang et al[18] conducted a study on patients undergoing total knee arthroplasty, who received clonidine for patient-controlled epidural analgesia. Less postoperative pain was seen in clonidine groups.

The limitation the study is small sample size.

Conclusion

Authors found that there was an increase in the duration of analgesia following the addition of clonidine to bupivacaine 2 ug/kg in comparison to bupivacaine alone when instilled in the epidural space.

References

1. Bonnet F, Brun-Buisson V, Saada M, et al. Dose-related prolongation of hyperbaric tetracaine spinal anesthesia by clonidine in humans. Anesth Analg 1989;68:619-22.

2. Nishikawa T, Dohi S. Clinical evaluation of clonidine added to lidocaine solution for epidural anesthesia. Anesthesiology 1990; 73:853-9.
3. Mogensen T, Eliasen K, Ejlersen E, et al. Epidural clonidine enhances postoperative analgesics from a combined low-dose epidural bupivacaine and morphine regimen. Anesth Analg 1992;75:607-10.
4. Yaksh TL, Reddy SVR. Studies in the primate on the analgetic effects associated with intrathecal action of opiates, alpha adrenergic agents and baclofen. Anesthesiology 1981;59:743-50.
5. Yaksh TL. Pharmacology of spinal adrenergic systems which modulate spinal nociceptive processing. Pharmacol Biochem Behav 1985;22:845-58.
6. Castro MI, Eisenach JC. Pharmacokinetics and dynamics of intravenous, intrathecal, and epidural clonidine in sheep. Anesthesiology 1989;71:418-25.
7. Fogarty DJ, Carabine UA, Milligan KR. Comparison of the analgesic effects of intrathecal clonidine and intrathecal morphine after spinal anaesthesia in patients undergoing total hip replacement. Br 1 Anaesth 1993;71:661-4.
8. Fijos K, Goudas LC, Patroni 0, Eolyzou V. Intrathecal clonidine as a sole analgesic for pain relief after cesarean section. Anesthesiology 1992;77:267-74.
9. De Kock M, Crochet B, Morimont C, Scholtes JL. Intravenous or epidural clonidine for intra- and postoperative analgesia. Anesthesiology 1993;79:525-31.
10. Eisenach JC, Lysak SZ, Viscomi CM. Epidural clonidine analgesia following surgery: phase 1. Anesthesiology 1989;71:640-6.
11. Eisenach JC, Rauck RL, Buzzanell C, Lysak SZ. Epidural clonidine analgesia for intractable cancer pain. Anesthesiology 1989;78:647-52.
12. Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anaesthesiol Stand Suppl 1965;16:55-69.
13. Eisenach JC, Tong C. Site of hemodynamic effects of intrathecal a,-adrenergic agonists. Anesthesiology 1991;74:766-71.
14. Arora P, Joseph J, Upadya M, Bhat S. Epidural clonidine as an adjuvant to local anesthetic in lower abdominal and lower limb surgeries: A randomised controlled study. The Open Anesthesia Journal. 2020 Feb 14;14(1).
15. Klimscha W, Chiari A, Krafft P, Plattner O, Taslimi R, Mayer N, Weinstabl C, Schneider B, Zimpfer M. Hemodynamic and analgesic effects of clonidine added repetitively to continuous epidural and spinal blocks. Anesthesia & Analgesia. 1995 Feb 1;80(2):322-7.
16. Fukuda T, Dohi S, Naito H. Comparisons of tetracaine spinal anesthesia with clonidine or phenylephrine in normotensive and hypertensive humans. Anesth Analg 1994;78:106-11.
17. Cucchiaro G, Adzick SN, Rose JB, Maxwell L, Watcha M. A comparison of epidural bupivacaine-fentanyl and bupivacaine-clonidine in children undergoing the Nuss procedure. Anesth Analg 2006; 103(2): 322-7.
18. Huang YS, Lin LC, Huh BK, *et al.* Epidural clonidine for postoperative pain after total knee arthroplasty: A dose-response study. Anesth Analg 2007; 104(5): 1230-5.