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ORIGINAL RESEARCH

SIMULTANEOUS USE OF DEXMEDETOMIDINE AND CLONIDINE AS POTENT ADJUVANT TO ROPIVACAINE FOR EPIDURAL ANESTHESIA IN LOWER LIMB AND LOWER ABDOMINAL SURGERIES; A COMPARATIVE STUDY

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ABSTRACT

Background: The potential and duration of analgesia can be increased by adding a suitable alpha 2 adrenergic agonists as adjuvants to ropivacaine during elective lower limb surgical procedures under epidural anaesthesia. Still there is a scope for research on the effects of clonidine and dexmedetomidine as potent adjuvants in epidural local anesthetics. The aim of our study is to compare the effect of clonidine and dexmedetomidine when used as an adjuvant to epidural ropivacaine in lower abdominal and lower limb surgeries.

Materials and Methods: Patients were randomized into fourgroups Group R (n=30) patients received 10ml of 1% isobaric ropivacaine alone, Group RC (n=30) patients received 10ml of 1% isobaric ropivacaine with clonidine 1µg/kg, Group RD (n=30) patients received 10ml of 1% isobaric ropivacaine with Dexmedetomidine 1µg/kg, Group RCD (n=30) patients received 10ml of 1% isobaric ropivacaine with 0.5µg/kg Dexmedetomidine and 0.5µg/kg of clonidine. Onsetofsensory analgesia using colds wab, onset of motor blockade using Bromage scale, time to 2 dermatome regression of sensory level, time to first demand for analgesia, sedationusing Ramsaysedation scale, intra operative hemodynamic parameters and complication swere assessed.

Results: The impressive and practically applicable results were obtained in Group RCD with respect to Results: The impressive and practically applicable results were obtained in Group RCD with respect to time for onset of analgesia (29 ± 3.9 sec), maximum sensory level (T 4.12 ± 1.1), time to peak sensory level (3.49 ± 1.2 min), time for two segment sensory regression (150 ± 12.3min), time taken for sensory regression to s1

(372.5 ± 17.1), duration of analgesia (439.3 ± 64.6 min), regression to Bromage 0 (41±11.3), onset to Bromage 3 (390 ± 32.9 min) and vas score (3.10±0.50).
Conclusion: The study results strongly conclude the use of 0.5µg/kg Dexmedetomidine and 0.5µg/kg of clonidine as aneffective adjuvant to10ml of 1% isobaric ropivacaine forepiduralanesthesia in lower limb and lower abdominal surgeries.
Keywords: Abdominal surgeries, Ropivacaine, Dexmedetomidine, sensory level, Bromage.

INTRODUCTION

Providing comfort to the patient by prevention and relief of pain and monitoring and maintenance of normal physiology through the operative period is the primary goal of an anaesthetist.[1] Epidural blockade is becoming one of the most useful and versatile procedures in modern anesthesiology used both for providing anesthesia and postoperative analgesia. It contributes to intra operative hemodynamic stability and has shown to reduce perioperative stress response thereby causing a decrease in complications and improving patient outcome. It helps in early mobilization by relieving postoperative pain, which decreases the incidence of thromboembolic events,[2-6] cardio toxicity and lesser motor blockade. Ropivacaine is being increasingly used in comparison to bupivacaine due to similar analgesic properties. A slightly larger dose of ropivacaine may be required,[7-9] but the quality and duration of analgesia is improved when a local anesthetic is combined with alpha 2 adrenergic agonists. Both clonidine and dexmedetomidine are alpha 2 adrenergic agonists, which have analgesic properties and potentiate local anesthetic effects.[10-12] Neuraxial clonidine, enhances the action of local anesthetics, increases the intensity and duration of analgesia. It is known to have sedative properties and the side effects are hypotension and bradycardia.[13-16] Dexmedetomidine is about 8 times more selective towards the alpha 2 adrenoreceptor than clonidine and hence allows the use of higher doses with less alpha 1 effect. It has been found to have hemodynamic stability, sedative, anxiolytic, analgesic, neuroprotective and anesthetic sparing effect. It causes more intense motor blockade and co-operative sedation without,[17-19] Increasing the incidence of side effects. The anaesthetic and the analgesic requirement get reduced to a huge extent by the use of these two adjuvants because of their analgesic properties and augmentation of local anaesthetic effects as they cause hyperpolarisation of nerve tissues by altering transmembrane potential and ion conductance at locus coeruleus in the brainstem,[20-25] the stable haemodynamics and the decreased oxygen demand due to enhanced sympathoadrenal stability make them very useful pharmacologic agents.[26,27] Very limited literature is available on the use of dexmedetomidine and clonidine as an adjuvant drug with ropivacaine in epidural analgesia. This study appears to be the first comparing combined effect of these drugs in epidural analgesia and thus keeping in mind their pharmacologic interactions and other properties the authors aimed the present comparative observational controlled study to link the effect of clonidine and dexmedetomidine when given either individually or in combination of these two as an adjuvant to ropivacaine in epidural anesthesia.

MATERIALS & METHODS

A comparative observational controlled study was planned. 120 patients of ASA I & II physical status aged between 18-60 yrs admitted for elective lower limb and lower abdominal surgeries. All subjects were satisfied all the inclusion criteria were enrolled in the study and were randomly allocated into four groups.

Group R (n=30) = patients received 10ml of 1% isobaric ropivacaine alone.

Group RC (n=30) = patients received 10ml of 1% isobaric ropivacaine with clonidine 1µg/kg.

Group RD (n=30) = patients received 10ml of 1% isobaric ropivacaine with Dexmedetomidine 1µg/kg Group RCD (n=30) = patients received 10ml of 1% isobaric ropivacaine with 0.5µg/kg Dexmedetomidine and 0.5µg/kg of clonidine.

The onsetofsensory analgesia using colds wab, onset of motor blockade using Bromage scale, time to 2 dermatome regression of sensory level, time to first demand for analgesia, sedation using Ramsay sedation scale, intra operative hemodynamic parameters and complications were assessed. The data obtained was subjected to statistical computation using statistical package for social science (SPSS) version 20.0 and value of $P < 0.05$ was considered significant and $P < 0.0001$ as highly significant.

Inclusion criteria:

1. ASA grade I & II status.
2. 18-60 years of age.
3. Patients giving informed written consent.
4. Patients scheduled to undergo elective below umbilical and lower limb surgical procedures under epidural anaesthesia.

Exclusion criteria:

1. ASA III or greater.
2. Age more than 60 years and less than 18 years.
3. Pregnant and lactating women.
4. Any contraindication to epidural anaesthesia –uncooperative patients, hypotension, previous spinal surgeries, spine abnormalities, local site infection and coagulation abnormalities.
5. Poorly controlled hypertension, angina, and cardiopulmonary disease.
6. Patients with haematological disease, neurologic, psychiatric disease, severe renal or hepatic derangement.
7. Patients taking Tricyclic antidepressants, any antipsychotic drugs, alpha-2 adrenergic agonists, opiods, antiarrhythmic, beta blockers, anticoagulants.

RESULTS

The demographic profile of study subjects as observed from [Table]1 the mean age group was maximum in Group RCD (36.52 ± 3.08) followed by Group RC (35.21 ± 2.8), Group RD (31.11 ± 4.70) and Group R (22.6 ± 3.2) respectively. The mean body weight was recorded maximum in Group RD (78.7± 1.3) followed by Group R (70.7 ± 2.3) Group RC (65.4 ± 6.6), and least in Group RCD (59.8 ± 5.6). The mean height was maximally in Group RC (156.3 ± 4.5) and Group R individuals were with high mean BMI (25.6 ± 2.1). At present study had high male to female ratio in Group RCD (25:5) were as the mean ASA I to II score ratio was

high in Group RC (22:8). The duration of surgery was comparatively high in Group RCD (100.33±23.64). [Table 1]

Table 1: Demographic characteristics

Variable	Group R (n=30)	Group RC (n=30)	Group RD (n=30)	Group RCD (n=30)	P value
Mean Age (y)	22.6 ± 3.2	35.21 ± 2.8	31.11 ± 4.70	36.52 ± 3.08	0.45
Mean Weight (kg)	70.7 ± 2.3	65.4 ± 6.6	78.7 ± 1.3	59.8 ± 5.6	0.06
Mean Height (cm)	155.9 ± 4.4	156.3 ± 4.5	149.9 ± 4.4	152.3 ± 4.5	0.73
Mean BMI (kg/m2)	25.6 ± 2.1	24.4 ± 2.9	24.6 ± 2.6	24.4 ± 2.9	0.82
Male :female ratio	20:10	22:8	21:9	25:5	0.08
Duration of surgery	88.33±23.64	95.33±23.99	99.65±2.57	100.33±23.64	0.09
ASA score I and II ratio	20:10	22:8	18:12	21:9	0.06

The maximum sensory levels obtained in study groups were comparable and sufficient for the surgery with Peak sensory level was achieved earlier in Group RCD (T 4.12 ± 1.1) followed by Group RD (T 5.9± 2.5), Group RC (T 6.99 ± 5.2) compared to Group R (T 7.9 ± 1.4) (p = 0.001). The time for analgesia onset was significantly rapid in Group RCD (29 ± 3.9) followed byGroup RD (32 ±11.3), Group RC (40±11.1) compared to Group R (68 ± 11.3) (p = < 0.001).

Table 2: Comparative block characteristics in two groups

Repression parameters	Group R (n=30)	Group RC (n=30)	Group RD (n=30)	Group RCD (n=30)	P value
Time for onset of analgesia (sec)	68 ± 11.3	40 ±11.1	32 ±11.3	29 ± 3.9	< 0.001
maximum sensory level	T 7.9 ± 1.4	T 6.99 ± 5.2	T 5.9 ± 2.5	T 4.12 ± 1.1	0.001
Time to peak sensory level (min)	5.98 ± 1.6	4.85 ± 2.6	4.01 ± 1.1	3.49 ± 1.2	0.023
Time for two segment sensory regression (min)	89.15 ± 6.5	126 ± 10.3	139 ± 13.3	150 ± 12.3	< 0.001
Time taken for sensory regression to S1 (min)	129.3 ±10.4	291.5 ± 11.2	321 ± 14.2	372.5 ± 17.1	< 0.001
Duration of analgesia (min)	85.9 ± 11.1	412.3 ± 14.6	429.2 ± 22.6	439.3 ± 64.6	< 0.001
Regression to Bromage 0 (min)	71.25± 11.3	54 ±11.3	49.6 ± 2.8	41±11.3	< 0.001

Onset to Bromage 3 (min)	113.2 ± 11.6	329 ± 21.9	342 ± 26.7	390 ± 32.9	< 0.001
VAS score	6.81±2.50	4.59±1.50	4.01±0.50	3.10±0.50	<0.001

The mean time for two segment sensory regression was significantly prolonged in Group RCD (150 ± 12.3) followed by Group RD (139 ± 13.3), Group RC (126 ± 10.3) compared to Group R (89.15 ± (p <0.001). The time taken for sensory regression of the blockade to S1 level was highest in Group RCD (372.5 ± 17.1) followed by Group RD (321 ± 14.2), Group RC (291.5 ± 11.2) compared to Group R (129.3 ±10.4) (p < 0.001). 24 hours postoperative VAS scores were consistently low in Group RCD (3.10±0.50) followed by Group RD (4.01±0.50), Group RC (4.59±1.50) compared to Group R (6.81±2.50) (p < 0.001). The mean duration of analgesia was recorded more in Group RCD (439.3 ± 64.6) followed by Group RD (429.2 ± 22.6), Group RC (412.3 ± 14.6) compared to Group R (85.9 ± 11.1) (p <0.001). The time of onset of Bromage Grade o min was rapid in Group RCD (41±11.3) followed by Group RD (49.6 ± 2.8), Group RC (54 ±11.3) compared to Group R (71.25± 11.3) (p <0.001). Whereas the time of onset of Bromage Grade 3 min was rapid onset in Group RCD (390 ± 32.9) followed by Group RD (342 ± 26.7), Group RC (329 ± 21.9) compared to Group R (6.81±2.50) (p <0.001).

Table 3 – Adverse effects

Adverse effect	**Group R (n=30)**	**Group RC (n=30)**	**Group RD (n=30)**	**Group RCD (n=30)**	**P value**
Nausea	8 (26.66%)	4 (6.66%)	3 (26.66%)	4 (30%)	0.001
Vomiting	3 (10.1%)	5 (6.66%)	3 (10.1%)	2 (16.66%)	0.05
Pruritus	4 (13.33%)	0 (0%)	1 (3.33%)	1 (3.33%)	0.05
Hypotension	8 (26.66%)	0(0%)	0 (0%)	0 (0%)	1
Shivering	0 (0%)	1 (3.33%)	0 (0%)	0 (0%)	.32
Bradycardia	5 (16.66%)	2(6.66%)	0 (0%)	0 (0%)	1
Pain	0 (0%)	1 (3.33%)	1 (3.33%)	2 (6.66%)	0.07
Total	28 (93.33%)	13 (43.33%)	9 (30%)	8 (26.66%)	0.17

The incidence of adverse effects varies among observable groups (table 3). Both the groups were observed for occurrence of possible adverse effects like nausea, vomiting, pruritus, shivering, hypotension, bradycardia and pain. Incidence of these adverse effects were low and not significant in Group RCD (26.66%), Group RD (30%) and Group RC (43.33%)but significant in Group R (93.33%)..

DISCUSSION

The combined use of these two drugs (clonidine and Dexmedetomidine) along with isobaric ropivacaine in lower abdominal and lower limb surgeries has not been extensively studied hence; the present trial was conducted to study the efficacy of addition of dexmedetomidine and clonidine in various combinations epidural isobaric ropivacaine for elective lower limb

and abdominal surgeries. Lower abdominal surgeries are performed under epidural anaesthesia is feasible for analgesia. Epidural ropivacaine alone has minimal duration of post-operative analgesia, by combining with adjuvants the duration of analgesia strongly prolongs. This study appears to be the first comparing combined effect of these drugs in epidural analgesia and we could not compare our results. Thus keeping in mind their pharmacologic interactions and other properties the authors aimed the present comparative observational controlled study to link the effect of clonidine and dexmedetomidine when given either individually or in combination of these two as an adjuvant to ropivacaine in epidural anesthesia during elective lower limb and lower abdominal surgeries. [Table 2]

CONCLUSION

The study outcome concludes that using 10ml of 1% isobaric ropivacaine with 0.5μg/kg dexmedetomidine and 0.5μg/kg of clonidine has rapid onset of sensory and motor blockade succeeded by ropivacaine with dexmedetomidine and ropivacaine with clonidine. The simultaneous use of ropivacaine+dexmedetomidine+clonidine in lower abdominal and lower limb surgeries has major advantages of prolonged sensory and motor blockade with impressive post-operative analgesia in prolonged and early onset of sensory and motor blockage duration and has better post-operative analgesia when compared to ropivacaine with dexmedetomidine, ropivacaine with clonidine, and ropivacaine alone.

REFERENCES

1. G Edward Morgan, Maged S Mikhail, Michael J Murray. The practice of Anesthesiology. Clinical Anesthesiology. 4th ed. McGrawHill,2008;1-16.
2. Nimmo SM. Benefit and outcome after epidural analgesia.Contin Educ Anaesth Crit Care Pain 2004;4:44-7.
3. Park WY, Thompson JS, Lee KK. Effect of epidural anesthesia and analgesia on perioperative outcome: A randomized, controlled Veterans Affairs cooperative study. Ann Surg 2001;234:560-9.
4. Holte K, Kehlet H. Epidural anesthesia and analgesia — Effects on surgical stress responses and implications for postoperative nutrition. Clin Nutr 2002;21:199-206.
5. Rigg JR, Jamrozik K, Myles PS, Silbert BS, Peyton PJ, Parsons RW, et al. Epidural anesthesia and analgesia and outcome of major surgery: A randomised trial. Lancet 2002;359:1276-82.
6. Moraca RJ, Sheldon DG, Thirlby RC. The role of epidural anesthesia and analgesia in surgical practice. Ann Surg 2003;238:663-73.
7. Chandran S, Hemalatha S, Viswanathan P. Comparison of 0.75% ropivacaine and 0.5% bupivacaine for epidural anesthesia in lower extremity orthopaedic surgeries. Indian J Anaesth 2014;58:336-8.
8. Markham A, Faulds D. Ropivacaine. A review of its pharmacology and therapeutic use in regional anesthesia.Drugs 1996;52:429-49.
9. Wahedi W, Nolte H, Witte P. Ropivacaine in epidural anesthesia. Dose-response relationship and a comparison with bupivacaine. Reg Anaesth 1990;13:57-65.

10. Förster JG, Rosenberg PH. Clinically useful adjuvants in regional anesthesia. Curr Opin Anaesthesiol 2003;16:477-86.
11. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, et al. Dexmedetomidine and clonidine in epidural anesthesia: A comparative evaluation. Indian J Anaesth 2011;55:116-21.
12. Swami SS, Keniya VM, Ladi SD, Rao R. Comparison of dexmedetomidine and clonidine (a2 agonist drugs) as an adjuvant to local anesthesia in supraclavicular brachial plexus block: A randomised double-blind prospective study. Indian J Anaesth 2012;56:243-9.
13. Eisenach J, Detweiler D, Hood D. Hemodynamic and analgesic actions of epidurally administered clonidine. Anesthesiology 1993;78:277-87.
14. Klimscha W, Chiari A, Krafft P, Plattner O, Taslimi R, Mayer N, et al. Hemodynamic and analgesic effects of clonidine added repetitively to continuous epidural and spinal blocks. Anesth Analg 1995;80:322-7.
15. Castro MI, Eisenach JC. Pharmacokinetics and dynamics of intravenous, intrathecal, and epidural clonidine in sheep. Anesthesiology 1989;71:418-25.
16. Eisenach JC, De Kock M, Klimscha W. Alpha (2)-adrenergic agonists for regional anesthesia. A clinical review of clonidine (1984-1995). Anesthesiology 1996;85:655-74.
17. Grewal A. Dexmedetomidine: New avenues. J Anaesthesiol Clin Pharmacol 2011;27:297-302.
18. Eisenach JC, Shafer SL, Bucklin BA, Jackson C, Kallio A.Pharmacokinetics and pharmacodynamics of intraspinal dexmedetomidine in sheep. Anesthesiology 1994; 80:1349- 59.
19. Sudheesh K, Harsoor S. Dexmedetomidine in anesthesia practice: A wonder drug? Indian J Anaesth 2011;55:323-4.
20. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology. 2000; 93:382–94.
21. Milligan KR, Convery PN, Weir P. The efficacy and safety of epidural infusions of levobupivacaine with and without clonidine for postoperative pain relief in patients undergoing total hip replacement. Anesth Analg. 2000; 91:393–7.
22. Klimscha W, Chiari A, Krafft P. Hemodynamic and analgesic effects of clonidine added repetitively to continuous epidural and spinal blocks. Anesth Analg. 1995:80:3

    22–7.
23. Fukushima K, Nishimi Y, Mori K. The effect of epidural administered dexmedetomidine on central and peripheral nervous system in man. Anesth Analg. 1997; 84:S292.
24. Scheinin M, Pihlavisto M. Molecular pharmacology of alpha2 -adrenoceptor agonists.Baillièe's Clin Anaesth. 2000; 14:247–60.
25. Correa-Sales C. A hypnotic response to dexmedetomidine, an alpha-2 agonist, is mediated in the locus coeruleus in rats. Anesthesiology. 1992; 76:948–52.

26. Taittonen MT, Kirvelä OA, Aantaa R, Kanto JH. Effect of clonidine and dexmedetomidine premedication on perioperative oxygen consumption and haemodynamic state. Br J Anaesth. 1997; 78:400–6.
27. Buerkle H. Peripheral anti-nociceptive action of alpha2 -adrenoceptor agonists.Baillièe's Clin Anaesth. 2000; 14:411–8.