Original Research Article

A comparative study of subcutaneous dexmeditomidine versus clonidine as adjuvant to spinal anesthesia at tertiary health care center

Nilima Vijay Narode

Assistant Professor, Department of Anaesthesia, Rural Medical College, Loni, Ahmadnagar, Maharashtra, INDIA.
Email: nilimanarode@gmail.com

Abstract

Background: In spinal anaesthesia, local anesthetics are widely used in combination with adjuvants such as opioids, alpha agonists to shorten the onset of action, increase the quality of block, increase the duration of anesthesia and analgesia, and decrease the dose of local anesthetics.α2-Agonists like clonidine and dexmedetomidine have been used to prolong spinal anesthesia. Apart from sedation and analgesia, they also decrease the sympathetic tone and the stress responses to surgery and anesthesia. The aim of this study is to evaluate and compare subcutaneous dexmeditomidine versus clonidine as adjuvant to spinal anesthesia with respect to sensory and motor blockade, hemodynamic changes, and adverse effects at tertiary health care center. **Material and Methods:** This observational, randomized double blind clinical study was conducted in patients aged between 18 and 60 years, ASA grade I-II, scheduled for elective surgeries under spinal anesthesia. Patients were randomly divided on lottery basis into two groups of 35 each in two groups. **Results:** Total 70 patients were considered for this study. 35 patients were randomly distributed in each group. General demographic characteristics as age, gender (male/female), weight and ASA grade (I/II), duration of surgery was comparable in both groups. Average duration of surgery was 110.4±39.8 min in group D while it was 107.9±37.2 min in group C. Sensory block Highest level (thoracic) attained in group D in 6.88±1.1 min while same in in group C was in 7.66±0.8 min. A statistically significant difference was noted. Postoperative VAS scores were lower in group C for first 12 hours postoperatively when compared to group D. At 4 hrs. there was a statistically significant difference between group D and group C was noted, rest there was no statistically significant difference between group D and group C. The mean duration of postoperative analgesia, defined by the time for use of first rescue analgesic 838.10±348.22 minutes in group D and 816.67±230.48 minutes in group C. This difference was statistically significant with a P-value<0.05. **Conclusion:** Use of dexmedetomidine and clonidine as an adjuvant to spinal anesthesia has been associated with prolonged duration of block and improved post-operative analgesia without any associated hypotension or other adverse events.

Keywords: dexmedetomidine, clonidine, spinal anaesthesia, adjuvant, postoperative analgesia

***Address for Correspondence:**
Dr Nilima Vijay Narode, Assistant Professor, Assistant Professor, Department of Anaesthesia, Rural Medical College, Loni, Ahmadnagar, Maharashtra, INDIA.
Email: nilimanarode@gmail.com

Received Date: 06/11/2020 Revised Date: 10/12/2020 Accepted Date: 19/01/2021
DOI: https://doi.org/10.26611/10151733

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 11 March 2021

Spinal anaesthesia is a widely used regional anaesthetic technique, particularly advantageous for lower abdominal and lower limb surgeries. Generally intrathecal 0.5% bupivacaine with dextrose, is appropriate for 1.5-2-hour surgical procedures.[1] In subarachnoid blocks, local anesthetics are widely used in combination with adjuvants such as opioids, alpha agonists to shorten the onset of action, increase the quality of block, increase the duration of anesthesia and analgesia, and decrease the dose of local anesthetics. α2-Agonists like clonidine and

How to site this article: Nilima Vijay Narode. A comparative study of subcutaneous dexmeditomidine versus clonidine as adjuvant to spinal anesthesia at tertiary health care center. *MedPulse International Journal of Anesthesiology.* March 2021; 17(3): 107-111. http://medpulse.in/Anesthsiology/index.php

dexmedetomidine have been used to prolong spinal anesthesia. Apart from sedation and analgesia, they also decrease the sympathetic tone and the stress responses to surgery and anesthesia.[2,3] The pharmacologic properties of α-2 agonists like clonidine and dexmedetomidine have been used extensively in various routes. Epidural administration of these drugs is associated with sedation, analgesia, anxiolysis, hypnosis and sympatholysis.[4] Dexmedetomidine, an alpha 2 agonist, is used as a local anaesthetic adjuvant in both peripheral nerve blocks and neuraxial anaesthesia. Perineural dexmedetomidine when given with LAs for peripheral nerve block has shown to have prolonged duration of postoperative analgesia with other beneficial effects such as reducing the opioid consumption.[5] Clonidine is an imidazole derivative with selective partial agonist properties which inhibits nociceptive impulses by activation of postjunctional alpha-2 adrenoreceptor in the dorsal horn of spinal cord. In neuraxial blocks, it has a local effect on blockage of sympathetic outflow while in peripheral nerve blocks it prolongs duration of analgesia by hyperpolarisation of cyclic nucleotide gated cation channels.[6] Both drugs are widely tested for intrathecal, intravenous, local routes but less literature is available for subcutaneous route. The aim of this study is to evaluate and compare subcutaneous dexmeditomidine versus clonidine as adjuvant to spinal anesthesia with respect to sensory and motor blockade, hemodynamic changes, and adverse effects at tertiary health care center.

MATERIAL AND METHODS

This observational, randomized double blind clinical study was conducted in Department of Anaesthesia, Rural Medical college, Loni. Study duration was of 6 months (May 2019- November 2019). Institutional ethical committee approval was taken for present study.

Inclusion criteria

- Patients aged between 18 and 60 years
- ASA I-II
- Scheduled for elective surgeries.

Exclusion criteria

- Patients using alpha 2-adrenergic receptors antagonists, calcium channel blockers, angiotensin-converting enzyme inhibitors
- Dysrhythmia
- Body weight more than 120 kg
- Height <140 cm
- Post spinal surgeries, spinal deformity
- History of allergy to study drugs
- Pregnancy
- Coagulopathy
- Neurological disorder.

A written informed consent was taken from patients. Total 70 adult patients of American Society of Anaesthesiologists (ASA) physical status 1 and 2 in the age group of 18 to 60 years of either sex posted for elective lower abdominal surgeries under spinal anesthesia were considered for study.

Patients were randomly divided on lottery basis into two groups of 35 each:

- Group C: 1 mcg/kg of clonidine diluted to 1 ml with normal saline.
- Group D: 0.5 mcg/kg of dexmedetomidine diluted to 1 ml with NS.

The drug combinations were prepared by one anesthetist, and various observations were made by a second anesthesiologist who was involved after the procedure had been performed.

All patients were earlier examined in pre-anesthetic clinic 1 day prior to surgery. Routine investigations performed in each case including electrocardiogram (ECG), chest X-ray, serum electrolytes, blood sugar, blood urea, serum patients instructed to undergo overnight fasting after 12 midnight. Patients were premedicated with pantoprazole 40 mg and ondansetron 4 mg on the previous night. All procedures explained to patient in detail. After arrival of patient in OT baseline systolic BP and heart rate (HR) recorded by taking the mean of 3 consecutive reading taken 1 min apart. Preloading done with Ringer lactate solution at a dose of 20 ml/kg/body weight over 15 min and no premedication given. A 25-gauge Quinke spinal needle was used for spinal anaesthesia. After completion of injection, the patients immediately returned to the supine position. The subcutaneous adjuvant drug was prepared and injected in the forearm by a second anesthesiologist who was not involved in the study using 26-gauge ½ inch hypodermic needle immediately following spinal anaesthesia. Assessment of analgesia pain was assessed by visual analogue score (VAS). Duration of pain relief (effective analgesia) was defined as the time from the spinal injection to the first request for rescue analgesics, or VAS was >4 was recorded. Rescue analgesics consisted of intravascular injection of diclofenac sodium 75 mg and repeated after 12 h if needed with a maximum daily dose of 150 mg. Rescue doses of diclofenac were recorded. All durations were calculated in relation to the time of spinal injection. All duration calculated considering the time of spinal injection as time 0. Patients were shifted to the postoperative ward and observed till the administration of rescue analgesic (diclofenac sodium 75 mg IV, as per the patient demanded or VAS >4).

Occurrence of nausea and vomiting, pruritus, shivering, drowsiness, hypoxia (SO2 <90%) dry mouth, bradycardia, hypotension or respiratory depression (respiratory rate <8/min) recorded to know undesirable side effects. The

incidence of hypotension (arterial BP <20% of baseline or mean arterial pressure (MAP) <60 mmHg was treated with injection ephedrine 6 mg IV increments and bradycardia as HR <60/min was treated with atropine 0.6 mg IV stat. Nausea and vomiting were treated with injection ondansetron 4 mg IV. Shivering was treated with warm drapes and warm IV fluids. Data was collected in predesigned proforma. The statistical tests which were used to measure the outcome were ANOVA, Chi-square test and Turkey test.

RESULTS

Total 70 patients were considered for this study. 35 patients were randomly distributed in each group. General demographic characteristics as age, gender (male/female) , weight and ASA grade (I/II), duration of surgery was comparable in both groups. Average duration of surgery was 110.4±39.8 min in group D while it was 107.9±37.2 min in group C. Sensory block Highest level (thoracic) attained in group D in 6.88±1.1 min while same in in group C was in 7.66±0.8 min. A statistically significant difference was noted.

Table 1: Demographic and general characteristic

	Group D	Group C	P value
Age	42.3±10.6 years	41.1±11.7 years	
Gender (male/female)	19/16	18/17	
Weight	58.2±14.1 kgs	60.1±11.8 kgs	
ASA grade (I/II)	21/14	24/11	
Duration of surgery			
< 60 minutes	18	21	
60-100 minutes	11	10	
>100 minutes	6	4	
Average duration of surgery	110.4±39.8 min	107.9±37.2 min	
Sensory block Highest level (thoracic)	6.88±1.1	7.66±0.8	Significant
Time for attaining highest level	11.6±1.9 mins	11.9±2.1mins	

values are mean±standard deviations or numbers

Major hemodynamic parameters as heart rate (mean heart rate, lowest heart rate, incidence of bradycardia), blood pressure (systolic, diastolic, mean arterial pressure) were compared for intraoperative/postoperative periods. Complications associated with regional anaesthesia as postoperative shivering, postoperative nausea and vomiting were compared and found non-significant. Parameters in group D and group C were comparable with each other. We did not note any statistical difference amongst them.

Table 2: Comparison of intraoperative/postoperative hemodynamic parameters

Hemodynamic parameters/complications	Group D	Group C	P value
Intraoperative hemodynamic parameters			
Heart rate (beats/min)	65.9±5.8	70.9±6.3	Not significant
Lowest heart rate	59.6±4.8	62.1±5.8	Not significant
Bradycardia (<50 beats/min)	3/35	2/35	Not significant
Systolic blood pressure (mm of Hg)	109.8±21.1	111.4±15.8	Not significant
Lowest SBP (mm of Hg)	100.5±11.3	104.1±10.0	Not significant
Diastolic blood pressure (mm of Hg)	71.4±9.8	68.6±5.1	Not significant
Mean arterial pressure (mm of Hg)	85.1±9.2	88.9±6.8	Not significant
Postoperative hemodynamic parameters			
Heart rate	65.1±5.6	68.9±6.3	Not significant
Systolic BP (mm of Hg)	118.9±11.7	116.8±9.8	Not significant
Diastolic BP (mm of Hg)	68.7±9.5	72.4±8.6	Not significant
Mean arterial pressure (mm of Hg)	89.1±8.1	86.5±9.3	Not significant
Complications			
Postoperative shivering	1/35	2/35	Not significant
Postoperative nausea and vomiting	2/35	2/35	Not significant

[values are mean±standard deviations or numbers (%)]

Postoperative VAS scores were lower in group C for first 12 hours postoperatively when compared to group D. At 4 hrs. there was a statistically significant difference between group D and group C was noted, rest there was no statistically significant difference between group D and group C. The mean duration of postoperative analgesia, defined by the time for use of first rescue analgesic 838.10±348.22 minutes in group D and 816.67±230.48 minutes in group C. This difference was statistically significant with a P-value<0.05.

Table 3: Postoperative VAS score

Group	Group D	Group C	P value
0 hrs.	0.00±0.00	0.00±0.00	Not significant
4 hrs.	2.46±0.41	2.33±0.61	Significant
8 hrs.	2.89±0.72	2.64±0.52	Not significant
12 hrs.	3.03±0.91	2.78±0.81	Not significant
16 hrs.	3.25±1.03	3.02±1.01	Not significant
20 hrs.	3.21±1.12	3.01±0.98	Not significant
24 hrs.	3.19±0.91	2.91±0.61	Not significant

DISCUSSION

Dexmedetomidine is a 7 times more selective alpha-2 receptor agonist in comparison to clonidine and has a similar mechanism of blocking hyperpolarisation activated cation channels.[7] Dexmedetomidine as an additive to intrathecal hyperbaric bupivacaine to prolong the quality and duration of action, probably it acts by binding to post-synaptic dorsal horn neurons and to the c-fibers in the presynaptic region and decreasing the release of c-fiber neurotransmitters producing hyperpolarization of neurons in the post-synaptic region.[8] Use of clonidine in neuraxial blocks had been plagued by the adverse effects like sedation, bradycardia and hypotension, thus necessitating a gradual evolution to present day recommendations of lower dosages.[9] Intrathecal administration of clonidine has evolved in terms of dosing from the initial phases of higher doses (150 µg) to routine use of lesser doses (15-40 µg) in present day practice to avoid its cardiovascular adverse effects. Intrathecal Clonidine supplementation of local anesthetic solutions result in increased segmental spread of sensory block, delayed regression of such blocks and decrease the failure rate and analgesic supplementation required in various surgical subsets.[9,10] Clonidine being a partial α2-adrenergic agonist potentiates both sensory and motor block of local anesthetics. Its analgesic effect is mediated through activation of postsynaptic α2-receptors in the substantia gelatinosa of the spinal cord. It decreases the release of nociceptive substances from substantia gelatinosa by activating the descending inhibitory medullospinal pathways.[11] It has also peculiarly shown benefits in alcoholics undergoing surgery by preventing postoperative alcohol withdrawal symptoms.[12] The hemodynamics parameters among patients receiving either dexmedetomidine or clonidine were comparable to each other without incidence of significant bradycardia and hypotension. Similar findings were noted in an Indian study by Divya B Srinivas, Geetha *et al.*[13] with subcutaneous use of dexmedetomidine or clonidine. They did not find any improvement in the onset times of sensory and motor blockade with the use of SC alpha 2 agonists, in contrast to previous studies which used IV alpha 2 agonists. This could be because the slower rate of absorption of subcutaneously administered drugs, which results in a slow rise in plasma concentration of the drug in contrast to the IV route thereby resulting in much less hemodynamic instability and prolonged duration of analgesia could be attributed to the longer half-life of subcutaneously administered drugs.[13]A meta-analysis on intrathecal dexmedetomidine has shown that its use has been associated with prolonged duration of block and improved post-operative analgesia without any associated hypotension or other adverse events, especially when used at doses less than 5 µg.[14] Comparative evaluation of dexmedetomidine and clonidine has revealed the superiority of dexmedetomidine when used as an adjuvant for epidural or intrathecal administration.[15,16] Bajwa *et al.* showed in their study that dexmedetomidine was a better adjuvant than clonidine in epidural ropivacaine anesthesia for patient comfort, superior sedative and anxiolytic properties, intra-operative and postoperative analgesia.[15] Intraoperative administration of dexmedetomidine in lower concentrations has reduced the requirement of other anesthetic agents; fewer interventions to treat tachycardia; and a reduction in the incidence of myocardial ischemia.[17] Dexmedetomidine has been effectively used intravenously for the treatment and prevention of shivering following SA without any major adverse effects in several studies. Few trials have examined intrathecal dexmedetomidine for the prevention of post-SA shivering.[18] Clonidine and dexmedetomidine by inhibition of central thermoregulation and attenuation of hyperadrenergic response to peri-operative stress are known to prevent postoperative shivering.[19] Manal *et al.*[20] in a comparative study of epidural morphine and epidural dexmedetomidine used as adjuvant to levobupivacaine in major abdominal surgery, found that dexmedetomidine was a good alternative to morphine as an adjuvant to levobupivacaine in epidural anaesthesia in major abdominal surgeries. In present study no significant difference between subcutaneous clonidine and dexmedetomidine was noted with respect to intra-operative and postoperative hemodynamic characteristics, postoperative analgesia. A large-scale study is needed for more promising results.

CONCLUSION

Use of dexmedetomidine and clonidine as an adjuvant to spinal anesthesia has been associated with prolonged duration of block and improved post-operative analgesia without any associated hypotension or other adverse events. However, among the two drugs, dexmedetomidine would provide a longer duration of analgesia along with intraoperative sedation than clonidine along with less side effects.

REFERENCES

1. Mikko Pitkänen. Spinal (Subarachnoid) blockade. In: Cousin MJ, Bridenbaugh PO, Carr DB, Horlocker TT, editors. Neural Blockade in Clinical Anaesthesia and Management of Pain. 4th ed. Philadelphia: Lippincot Williams and Wilkins; 2009. p. 213-38.
2. Elcicek K, Tekin M, Kati I. The effects of intravenous dexmedetomidine on spinal hyperbaric ropivacaine anesthesia. J Anesth 2010;24:544-8.
3. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Jazzar MD, Alameddine MM, Al-Yaman R, *et al.*. Effects of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anesthesiol Scand 2006;50:222-7.
4. Mauro VA, Brandao ST. Clonidine and dexmedetomidine through epidural route for postoperative analgesia and sedation in a cholecystectomy. Rev bras Anestesiol 2004;4:1-10.
5. Abdallah FW, Brull R. Facilitatory effects of perineural dexmedetomidine on neuraxial and peripheral nerve block: A systematic review and meta-analysis. Br J Anaesth 2013;110:915-25.
6. Saxena AK, Arya SK. Current concepts in neuraxial administration of opioids and non-opioids: an overviewand future perspectives. *Indian J Anaesth* 2004; 48: 13-24.
7. Brummett CM, Hong EK, Janda AM, Amodeo FS, Lydic R. Perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolongs the duration of analgesia by blocking the hyperpolarization-activated cation current. *Anesthesiology* 2011; 115: 836-843
8. 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.
9. Dobrydnjov I, Axelsson K, Thörn SE, Matthiesen P, Klockhoff H, Holmström B, Gupta A. Clonidine combined with small-dose bupivacaine during spinal anesthesia for inguinal herniorrhaphy: a randomized double-blinded study. *Anesth Analg* 2003; 96: 1496-1503,
10. Davis BR, Kopacz DJ. Spinal 2-chloroprocaine: the effect of added clonidine. *Anesth Analg* 2005; 100: 559-565
11. Christiansson L. Update on adjuvants in regional anaesthesia. Period Biol 2009;61:161-70.
12. Dobrydnjov I, Axelsson K, Berggren L, Samarütel J, Holmström B. Intrathecal and oral clonidine as prophylaxis for postoperative alcohol withdrawal syndrome: a randomized double-blinded study. *Anesth Analg* 2004;
13. Divya B Srinivas, Geetha Lakshminarasimhaiah, Comparison of subcutaneous dexmedetomidine versus clonidine as an adjuvant to spinal anesthesia: a randomized double blind control trial, Local and Regional Anesthesia 2019:12 29–36
14. Niu XY, Ding XB, Guo T, Chen MH, Fu SK, Li Q. Effects of intravenous and intrathecal dexmedetomidine in spinal anesthesia: a meta-analysis. *CNS Neurosci Ther* 2013; 19: 897-904
15. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, Kulshrestha A, Singh A, Parmar S, Singh A, Goraya S. Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. *Indian J Anaesth* 2011; 55: 116-121
16. Mahendru V, Tewari A, Katyal S, Grewal A, Singh MR, Katyal R. A comparison of intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: A double blind controlled study. *J Anaesthesiol Clin Pharmacol* 2013; 29: 496-502
17. Aho M, Lehtinen AM, Erkola O, Kallio A, Korttila K. The effect of intravenously administered dexmedetomidine on perioperative hemodynamics and isoflurane requirements in patients undergoing abdominal hysterectomy. Anesthesiology 1991;74:997-1002.
18. Ellakany M, Abdelhamid SA, Girgis M. Intrathecal dexmedetomidine or meperidine for post spinal shivering. Int J Anesth Anesth. 2014;1(2):1:004.
19. Talke P, Tayefeh F, Sessler DI, Jeffrey R, Noursalehi M, Richardson C. Dexmedetomidine does not alter the sweating threshold, but comparably and linearly decreases the vasoconstriction and shivering thresholds. Anesthesiology 1997; 87:835-41.
20. Manal M. Kamal, Sahar M. Talaat Comparative study of epidural morphine and epidural dexmedetomidine used as adjuvant to levobupivacaine in major abdominal surgery Egyptian Journal of Anaesthesia. 2014 April; 30(2):137-141.

Source of Support: None Declared
Conflict of Interest: None Declared