

Comparative study of intrathecal bupivacaine and bupivacaine with clonidine in infra-umbilical surgeries

Sameer Goyal^{1*}, Smita Barya², Ankush Kumar Garg³

¹Associate Professor, MD Anaesthesiology, PDCC Cardiac Anaesthesiology, Pacific Medical College and Hospital (PMCH), Udaipur, Rajasthan, India

²Associate Professor, M.S Obs. and Gynae., Ananta Institute of Medical Sciences and Research Centre (A.I.M.S.R.C), Rajsamand, Rajasthan, India

³Assistant Professor, M.D Anaesthesiology, R.N.T Medical College, Udaipur, Rajasthan, India

Received: 19-10-2020 / Revised: 12-12-2020 / Accepted: 28-12-2020

Abstract

Introduction: Intrathecal clonidine is a safe, nonopioid adjuvant to local anaesthetics to prolong the duration of anaesthesia and analgesia without any major side effects. We investigated and compare the characteristics of spinal block, duration of postoperative analgesia, hemodynamic responses and side effects using intrathecal bupivacaine and its combination with clonidine in patients undergoing infra-umbilical surgeries. **Material and Methods:** In the present study, 70 patients of ASA grade I and II, age between 18-64 years were randomly allocated in two groups. Group A received 12.5 mg of hyperbaric 0.5% bupivacaine with 0.5 cc of normal saline and group B received 12.5 mg of hyperbaric 0.5% bupivacaine plus 75µg of clonidine. Various parameter of intrathecal block were than studied. **Result:** Addition of clonidine to 0.5% hyperbaric bupivacaine given intrathecally significantly prolonged the duration of motor blockade, time for two segment regression and the duration of postoperative analgesia with minimal acceptable side effects as compare to bupivacaine alone. **Conclusion:** Intrathecal addition of clonidine significantly prolongs the duration of motor block providing good postoperative analgesia as well as improves the quality of block.

Keywords: Intrathecal, Bupivacaine, Clonidine, Infra-umbilical, Sensory Block, Motor Block, Postoperative Analgesia.

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Since its introduction by “August Bier” in 1898, spinal anaesthesia is widely being practiced for providing sensory and motor block for lower limb surgeries due to its simplicity, minimum skill implementation, optimal operative condition, lowered risk of aspiration, low intra-operative blood loss, continued analgesia in the post-operative period and minimal postoperative morbidity. It is frequently used in infra-umbilical surgeries like lower extremity, lower abdominal surgeries[1]. The drugs used for subarachnoid block are bupivacaine, lignocaine etc. Bupivacaine only subarachnoid block is having a relatively short duration of action leading to early intraoperative need for supplemental intravenous analgesics and even general anaesthesia. Quality and duration of anaesthesia and postoperative analgesia can be improved by adding adjuvant drugs to local anaesthetic[2]. Demonstration of opiate receptors in the brain and substantia gelatinosa of spinal cord has revolutionized the concept of pain relief[3]. It was found that addition of clonidine as adjuvant in spinal

anaesthesia leads to decrease in the time of onset of block, increase its quality and duration of action, lowers the dose of local anaesthetic, reduce systemic absorption and therefore prevent its side effects[4]. So we undertook this study with aim to evaluate and compare the changes in characteristics of spinal blockade, postoperative analgesia and vital parameter due to bupivacaine and bupivacaine plus clonidine in infra-umbilical surgeries. We conducted the present study using clonidine as an adjuvant to bupivacaine with the aim to evaluate and compare the changes in characteristics of spinal blockade, postoperative analgesia and vital parameter due to bupivacaine and bupivacaine plus clonidine in infra-umbilical surgeries.

Material and Methods

After obtaining institutional ethics committee approval and written informed consent from all patients, present study was conducted on 70 patients of ASA grade I and II, aged between 18-64 years scheduled for infra-umbilical surgeries. Patients with systemic diseases and having contraindications for spinal anaesthesia were excluded from the study. Selected patients were divided into two equal groups of 35 patients each. A detailed pre-anaesthetic evaluation including history, thorough physical and clinical examination and all relevant investigations were done for all the patients. Patients were kept nil per oral for 8 hrs prior to the procedure. All patients were pre medicated with oral alprazolam 0.5 mg and

*Correspondence

Dr. Sameer Goyal,

Associate Professor, MD Anaesthesiology,
PDCC Cardiac Anaesthesiology, Pacific Medical College and
Hospital (PMCH), Udaipur, Rajasthan, India.

E-mail: sameergoy@yahoo.com

ranitidine 150 mg at night before surgery. Inside operation theater, all standard monitoring devices were attached to the patient and baseline parameters like blood pressure, pulse rate, SPO₂, along with respiratory rate were noted. A good intra-venous line was secured and patients were preloaded with 15 ml/kg of Ringer lactate. Under strict aseptic conditions lumbar puncture was performed in lateral position at the level of L3 –L4 or L4 –L5 inter-vertebral space using 25G spinal needle. After obtaining free flow of cerebrospinal fluid, study drug was injected intrathecally. Study groups received spinal anaesthesia with,

Group A: 12.5 mg hyperbaric 0.5% bupivacaine plus 0.5 ml normal saline intrathecally.

Group B: 12.5 mg hyperbaric 0.5% bupivacaine plus clonidine 75µg intrathecally.

Post spinal patients were placed in the supine position. The time of injection of drug, onset of sensory and motor block were noted in all patients. The parameters observed were quality of sensory and motor block, two segment regressions time, total duration of motor block, haemodynamic responses like pulse rate (PR), blood pressure (BP), respiratory rate (RR) and saturation (SpO₂) were monitored and recorded throughout the procedure. The highest level of sensory block was evaluated by pinprick at midclavicular line anteriorly every 5 min for 20 min after injection and there after every 30 min. The duration of sensory block was defined as the time of regression of two segments in the maximum block height, evaluated by pinprick. Motor block onset was assessed with bromage score. Time for motor block onset was assumed when bromage score becomes three. Modified

bromage scale was followed according to which: 0 – able to raise the whole lower limb at the hip, 1 – able to flex the knee but unable to raise the leg at hip, 2 – able to plantar flex ankle but unable to flex the knee, and 3 – no movement of lower limb. Complete motor block recovery was assumed when Bromage score became zero. The duration of spinal anaesthesia/mean time to analgesic request was defined as the period from spinal injection to the first occasion when the patient complained of pain in the postoperative period. Duration of post-operative analgesia, intensity of post-operative pain at rest and on movement were measured by visual analog scale, time for first dose of analgesic and perioperative complications as hypotension, nausea, dryness of mouth, sedation and respiratory depression were recorded. Hypotension was defined as a decrease in blood pressure by 20% from preoperative value.

Statistical analysis

All observations were recorded and student's t test was applied to test statistical significance between the means of the groups. The chi square test was used to find dependencies between the two groups. Data are presented as mean ±SD. P<0.05 was considered statistically significant and P < 0.001 was considered highly significant.

Results

A total of 70 patients who underwent infra-umbilical surgeries were enrolled for the study and were randomly allocated into 2 groups of 35 patients each. There were no intergroup differences as regards to the demographic profile and ASA physical status of patients enrolled in our study [Table 1].

Table-1: Demographic data

Variables	Group A (control)	Group B (Clonidine)
Age (years)	36.43 ± 4.32	36.58 ± 4.27
Weight (kg)	5.950 ± 5.39	58.68 ± 4.90
Height (cm)	157.40 ± 4.80	158.57 ± 3.96

Table-2: Summary of results of spinal blockade and duration of analgesia

Characteristics (minutes)	Group A	Group B	
Time of two segment regression	127 ± 5.36	205 ± 4.88	P< 0.01
Duration of motor blockade	159 ± 3.48	208 ± 3.35	P< 0.05
Duration of analgesia	208 ± 4.39	498 ± 4.51	P< 0.01

Duration of motor blockade in patients receiving clonidine with bupivacaine intrathecally was more (208 mins) as compared to bupivacaine alone (159 mins) and the difference was statistical significant, P< 0.05. The time for two segment regression in clonidine group was 205 minutes in comparison to 127 minutes for control group, which was statistically significant (P< 0.01). The duration of post-operative analgesia in clonidine group was 498 minutes which was

higher than that in control group 208 minutes (P< 0.01), thus reduced need for post-operative analgesic requirement. The results regarding characteristics of intrathecal blockade and duration of analgesia are shown in Table 2.

Hypotension was observed in clonidine group especially after 40 minutes of intrathecal administration. This fall in blood pressure was not more than 15% of preoperative values (fig. 1).

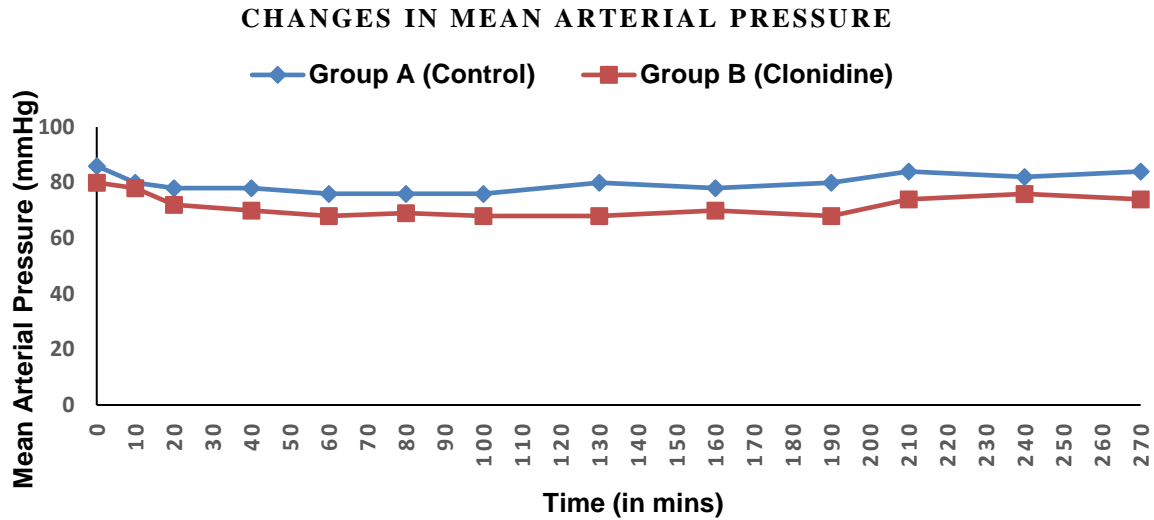


Fig 1: Comparison of changes in mean arterial pressure in both groups

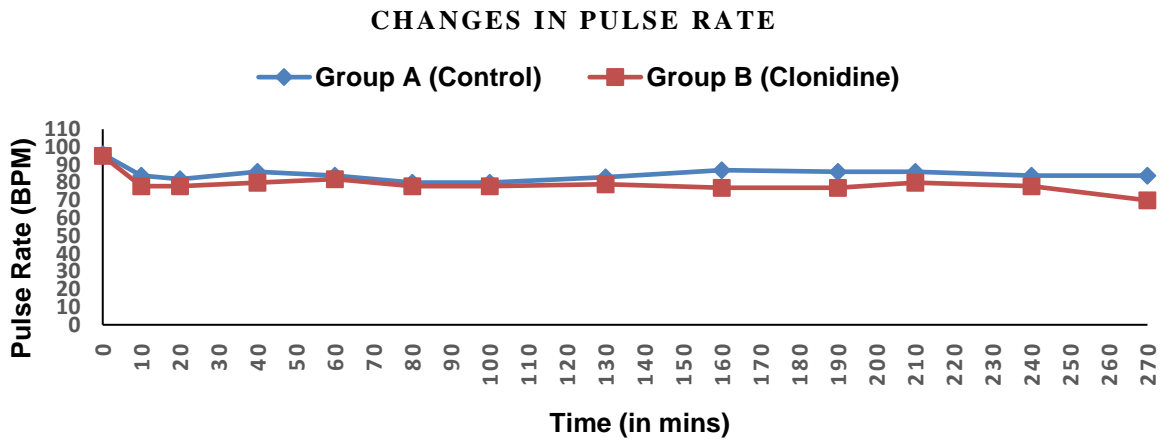


Fig 2: Comparison of changes in pulse rate in both groups

Changes in pulse rate at different time intervals in both the groups is shown in figure 2. On comparing two groups, clonidine group showed decrease in pulse rate as compare to control group.

Side effects observed in the study are shown in Table 3. 15 patients belonging to the clonidine group had dryness of

mouth whereas only 4 patients from control group. 22 patients from the clonidine groups were sedated (sedation score 1-2) but none from the bupivacaine group, thus decreasing the sedative requirement using clonidine as an adjuvant to bupivacaine.

Table 3: Showing complications observed in two groups

Complications	Group A	Group B
Dryness of mouth	4	15
Nausea	5	5
Sedation	0	22
Respiratory depression	0	0

Discussion

Below umbilicus surgeries are commonly performed under spinal anaesthesia using local anaesthetic agents. But their relatively short duration of action may lead to early analgesic requirement in the postoperative period[5,6]. Bupivacaine is one of the local anaesthetic given routinely for infra-umbilical surgeries. It provides adequate sensory and motor

blockade for surgery and also provides some pain relief in initial postoperative period. But as the duration of analgesia is not lengthy enough to relieve pain for extended period in postoperative settings it may increases morbidity. Adequate pain relief must be included in anaesthesia planning before induction of anaesthesia as it decreases fear, anxiety, reduces morbidity. To prolong the intraoperative as well as post-

operative analgesia, a number of adjuvant drugs to local anaesthetics has been used intrathecally.

Clonidine, an α_2 adrenergic agonist, is having sympatholytic, hypnotic, sedative, anxiolytic, analgesic and anaesthetic sparing effects without respiratory depression[7,8]. When given intrathecally as an adjuvant drug, it results in the prolongation of sensory and motor blockade and a reduction in the amount of local anaesthetic required to produce prolonged perioperative analgesia, thereby reducing the incidence of side effects. In our study, both groups were comparable in respect to demographic parameters. There is little, insignificant change in terms of onset and quality of sensory and motor block, time to reach maximum level of sensory block on addition of clonidine to bupivacaine.

Addition of clonidine to bupivacaine intrathecally prolongs duration of sensory and motor block and time for two segment regression significantly with minimal haemodynamic alterations. The results of our study are in accordance with observations of various studies which concluded that the duration of sensory and motor block was significantly prolonged by the addition of intrathecal clonidine[9-13]. The possible mechanisms involved in potentiating the sensory block include suppression of the activity of wide dynamic range of neurons and release of substance P in the dorsal horn of spinal cord by activation of pre and post-synaptic α_2 adrenergic receptors on small primary afferents; release of norepinephrine and acetylcholine in spinal cord dorsal horn; direct inhibition of impulse conduction in A delta and especially C fibers, possibly by increasing potassium conductance[14,15]. Clonidine causes motor block by inducing cellular modification in the ventral horn of spinal cord (motor neuron hyperpolarization) and potentiating the action of local anaesthetics. The time of analgesic request was significantly prolonged in clonidine groups. Our results are in agreement with the results of other studies which observed prolonged duration of spinal anaesthesia in clonidine group[9,16].

In terms of vital parameters, pulse rate decreases at various time intervals in clonidine group as compare to control group. There was potential hypotension observed in clonidine group especially after 40 minutes of intrathecal administration. B.S. Sethi et al[17], in his study showed a decrease in mean heart rate (from 45 minutes until the end of 6 hours) was greater in clonidine group than in the control group ($p < 0.001$). Negri et al[18] found that the addition of 105 mcg of clonidine to hyperbaric bupivacaine exerted minimal influence on hemodynamic parameters. Racle et al[19] found that maximum decrease in systolic blood pressure by intrathecal clonidine (105 mcg) was of only 15% from baseline values.

Incidence of sedation (assessed by sedation score) was higher in the clonidine group (22 patients) than in the control group and was statistically significant ($p < 0.001$). Sedation is a well-known side effect of clonidine but at the dose we used clonidine in our study, we did not notice any respiratory depression in any of our patients. Dryness of mouth, a typical side effect of clonidine was also reported in more patients in the clonidine group than control group[20].

Conclusion

We, therefore, concluded that the addition of 75 μg of clonidine to 0.5% hyperbaric bupivacaine intrathecally, significantly prolongs the duration of sensory and motor blockade along with prolonged and adequate postoperative analgesia with moderate sedation. These outcomes not only decrease the dose of bupivacaine required but also the need of sedatives and other analgesics with minimum acceptable side effects.

References

- Gentili M and Bonnet F. Spinal clonidine produces less urinary retention than spinal morphine. *British Journal of anaesthesia*. 1996;76:872-873.
- Bajwa SJS, Kaur J, Singh G et al. Dexmedetomidine and clonidine in epidural anaesthesia. *Indian J Anesth* 2011;55:116-121.
- Pert CB, Snyder SH. Opiate receptor: Demonstration in nervous tissue. *Science* 1973 ;179:1011-4.
- Barsagade WS, Tirpude NG and Yelne TS. Evaluation of addition of clonidine and dexmedetomidine to intrathecal hyperbaric bupivacaine for lower limb, sub umbilical surgeries. *Research Chronicle in health sciences* 2015;1:234-240.
- David LB. Spinal, epidural and caudal anesthesia. In: Miller RD, editor. *Miller's Anesthesia*, 6th ed, vol.2. Philadelphia: Churchill Livingstone; 2005. p.1653-1683.
- Local anesthetics. In: Collins VJ, editor. *Principle of Anesthesiology*. 3rd ed, Vol.2, Philadelphia: Lea and Febiger; 1993. p.1232-1281.
- Tryba M, Gehling M. Clonidine: A potent analgesic adjuvant. *Curr Opin Anaesthesiol*. 2002;15:511-517.
- Jamadarkhana S, Gopal S. Clonidine in adults as a sedative agent in the intensive care unit. *J Anaesthesiol Clin Pharmacol*. 2010;26:439-445.
- Dobrydnjov I, Axelsson K, Samaritel J, Holmström B. Postoperative pain relief following intrathecal bupivacaine combined with intrathecal oral clonidine. *Acta Anaesthesiol Scand* 2002;46:806-14.
- Singh RB, Chopra N, Choubey S, Tripathi R K, Prabhakar, Mishra A. Role of Clonidine as adjuvant to intrathecal bupivacaine in patients undergoing lower abdominal surgery: A randomized control study. *Anesth Essays Res* 2014;8:307-12.
- Strebel S, Gurzeler JA, Schneider MC, Aeschbach A, Kindler CH. Small-dose intrathecal clonidine and isobaric bupivacaine for orthopedic surgery: A dose-response study. *Anesth Analg* 2004;99:1231-8.
- Niemi L. Effects of intrathecal clonidine on duration of bupivacaine spinal anaesthesia, haemodynamics, and postoperative analgesia in patients undergoing knee arthroscopy. *Acta Anaesthesiol Scand* 1994;38:724-8.
- Merivirta R, Kuusniemi K, Jaakkola P, Pihlajamäki K, Pitkänen M. Unilateral spinal anaesthesia for outpatient surgery: A comparison between hyperbaric bupivacaine and bupivacaine-clonidine combination. *Acta Anaesthesiol Scand* 2009;53:788-93.
- Yaksh TL. Pharmacology of spinal adrenergic systems which modulate spinal nociceptive processing. *Parmacol Biochem Behav* 1985; 22:845-58.

15. Reddy SV, Yaksh TL. Spinal noradrenergic terminal system mediates antinociception. *Brain Res* 1980;189:391-401.
16. Saxena H, Singh S, Ghildiyal S. Low dose intrathecal clonidine with bupivacain improves onset and duration of block with haemodynamic stability. *Internet J Anesthesiol* 2010;23:9137.
17. Sethi BS, Samuel M, Sreevastava D. Efficacy of analgesic effect of low dose intrathecal clonidine as adjuvant to bupivacaine. *Indian Journal of Anaesthesia* 2007;51:415-419.
18. De Negri P, Salvatore R, Visconti C, De Vivo P, Mastronardi P. Spinal anaesthesia with clonidine and bupivacaine in young humans: interactions and effects on cardiovascular system. *Minerva Anesthesiology*. 1997;63:119-125.
19. Racle JP, Benkhadra A, Poy JY, Gleizal B. Prolongation of isobaric bupivacaine spinal anaesthesia with epinepherine and clonidine for hip surgery in elderly. *Anesth Analg* 1987;66:442-446.
20. Gordh T Jr. Epidural clonidine for treatment of postoperative pain afterthoracotomy. A double blind placebo-controlled study. *Acta Anaesthesiol Scand*. 1988;32:702-709.

Conflict of Interest: Nil

Source of support: Nil