

Comparative Efficacy of Intrathecal Bupivacaine Alone and Combination of Bupivacaine with Clonidine in Spinal Anaesthesia

AJAY WAHI¹, AMANJOT K. SINGH², KARTIK SYAL³, AJAY SOOD⁴, JYOTI PATHANIA⁵

ABSTRACT

Introduction: Clonidine is an α_2 agonist agent that has been used as an adjuvant to local anaesthetics in regional anaesthesia.

Aim: This study compared two combinations of bupivacaine and clonidine with bupivacaine alone for surgeries below the level of umbilicus in spinal anaesthesia.

Materials and Methods: We conducted a randomized double blind study on 90 patients of ASA I and ASA II aged 20-60 years, 30 in each group, undergoing surgery below the level of umbilicus in spinal anaesthesia. For intrathecal block, Group 1 received bupivacaine hydrochloride 12.5mg (2.5ml) in 8% dextrose (0.5% sensorcaine heavy) + 1ml (150 μ g) of preservative free clonidine. Group 2 received bupivacaine hydrochloride 12.5mg (2.5ml) in dextrose (0.5% sensorcaine heavy) + 0.5ml (75 μ g) of preservative free clonidine + 0.5ml of normal saline to make the volumes of all the groups same. Group 3 received bupivacaine hydrochloride 2.5ml in 8% dextrose (0.5% sensorcaine heavy) + 1ml of normal saline to make the volumes of all the groups

same. Heart rate, NIBP, oxygen saturation and respiratory rate were monitored. The onset and duration of sensory block, the highest dermatomal level of sensory block, motor block, time to complete motor block recovery and duration of spinal anaesthesia were recorded.

Statistical Analysis: The data of the study was recorded in the record chart and results were evaluated using statistical tests (ANOVA test, post-hoc turkey hsd test, paired t-test and chi-square test).

Results: Demographic data, the incidence and duration of bradycardia were comparable amongst the groups. The duration of sensory and motor block were greatest in group 1, followed by group 2 and group 3 ($p < 0.01$). Decrease in the systolic blood pressure of group 2 and group 3 was noted as compared to group 1. No significant sedation or respiratory depression was observed in any group.

Conclusion: Addition of clonidine to bupivacaine intrathecally is although a reliable method to prolong spinal anaesthesia but close monitoring for hypotension is desirable.

Keywords: Adjuvant, α_2 agonist, ASA 1&2, Bromage scale, Lower abdominal surgery, Subarachnoid block

INTRODUCTION

Spinal anaesthesia is being practiced safely and effectively since many years. Like most regional anaesthesia techniques it is easily administered and gives excellent surgical conditions [1,2]. But spinal anaesthesia using local anaesthetics has a limited duration of action that may result in conversion to general anaesthesia for completion of surgery. Similarly, combined spinal epidural anaesthesia has also been tried but it is technically more challenging [3], may not provide good surgical conditions and has its own side effects. Therefore, continuous research is going on to improve upon this most used regional anaesthetic technique. Tamsen and Gordh proved safety of parenteral preparation of clonidine for intrathecal use in humans [4]. Although, even large doses of clonidine intrathecally were inadequate to produce surgical anaesthesia [5], it repeatedly prolonged sensory and motor blockade when used as an adjuvant to local anaesthetics. Various studies used clonidine as adjuvant in different doses and with different local anaesthetics, but they have yielded conflicting results [5-7].

AIM

In this comparative study, the effects of bupivacaine alone and bupivacaine in combination with two different doses of clonidine were evaluated in patients undergoing surgery below the level of umbilicus in spinal anaesthesia.

MATERIALS AND METHODS

After the approval by the ethical committee of Indira Gandhi Medical College, Shimla, we conducted a randomized double blind study on 90 patients of either sex belonging to ASA physical status I and II, scheduled for surgery below the level of umbilicus in spinal anaesthesia over a period of six months. The patients with bradyarrhythmia, atrioventricular heart block, having epilepsy or depressive neurological disorder and other relative or absolute contraindications to spinal anaesthesia were excluded from the study. All the patients were informed of the procedure to be carried out on them in the operative and the recovery room and written consent was obtained. The patients were allotted to either of the 3 study groups of 30 patients each as per random number list. To achieve a double blind study, the trial drug was prepared, coded and administered by an anesthetist not otherwise participating in the study. Both, the patient as well the investigator observing the results, were blind to the test drug by giving serial numbers to the patients which were decoded at the end of the study. All observations were made by the same observer to eliminate subjective error.

All routine investigations were done prior to the surgery. All the patients were kept nil per oral for at least six hours prior to the surgery.

anaesthesia

Premedication in the form of tablet alprazolam 0.25mg was given on the night before the operation. After shifting the patient to operation theatre, baseline parameters like ECG, HR, NIBP,

RR, peripheral oxygen saturation (spO_2) were recorded by the candidate who was blinded to the adjuvant drug used. In the operation theatre intravenous line was secured in all patients and 5ml/kg of isotonic normal saline was given before giving subarachnoid block. Monitoring of the heart rate, ECG, NIBP and oxyhaemoglobin saturation was established. Under all aseptic conditions subarachnoid puncture was performed using midline lumbar approach, with patient in sitting position using 26 gauge Quincke needle in L_3-L_4 interspace and after confirmation of the free flow of CSF, drugs were given according to the three groups in a double blind way.

The various treatment groups were as under:

Group 1 - 2.5ml of 0.5% heavy bupivacaine + 1ml (150 μ g) of clonidine.

Group 2 - 2.5ml of 0.5% heavy bupivacaine + 0.5ml of normal saline + 0.5ml (75 μ g) of clonidine.

Group 3 - 2.5ml of 0.5% heavy bupivacaine + 1ml of normal saline.

The patients were then turned supine with no head tilt. Baseline values for monitored variables were taken. Heart rate, NIBP, oxyhaemoglobin saturation was monitored every minute for the first 10 minutes, every 5 minutes for the next 20 minutes and then at an interval of 15 minutes for one hour after subarachnoid block. Respiratory rate, level of sedation (Ramsay's scoring), grade of motor block (Bromage scale) and level of sensory block (pin prick test) were monitored every 1 hour after injecting the drug until end of the study. Level of sensory block was seen by pin prick method after 7 minutes of injecting the drug. Time taken for the onset of action was noted from the time of injecting the drug into subarachnoid space to complete analgesia at the level of lower border of umbilicus. Duration of sensory block was calculated as the time taken for regression to two lower levels compared to that at the onset, which was taken as end point of the study. Duration of motor block was calculated as the time from the onset of action to no block on Bromage scale. A fall of more than 30% in systolic arterial pressure of baseline value or a reading of less than 90 mm Hg was treated with an intravenous bolus of 6 mg of mephenteramine. Any episode of bradycardia (heart rate < 50/min) was treated with 0.6 mg of i.v. atropine.

STATISTICAL ANALYSIS

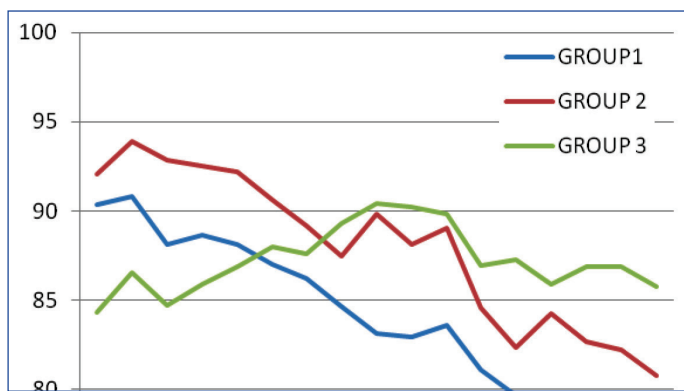
The data of the study was recorded in the record chart and results were evaluated using statistical tests (ANOVA test, post-hoc turkey hsd test, paired t-test and chi-square test).

RESULTS

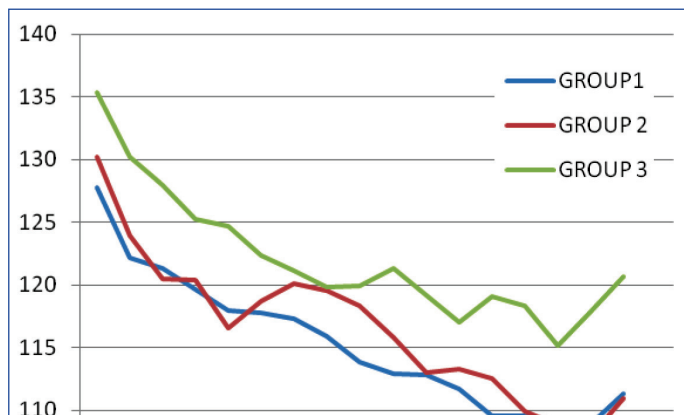
The age, sex and weight were comparable in all the three groups as shown in [Table/Fig-1]. The difference between baseline parameters was also insignificant. The time taken for the onset of action and the level of sensory block achieved was comparable in all groups. Although, the heart rate decreased significantly in group 2 and group 3 as compared to their baseline values, but it remained comparable when group 2 was compared to group 3 as shown in [Table/Fig-2]. Incidence of bradycardia was statistically insignificant. The systolic blood pressure showed significant decrease in all the groups as compared to the baseline value. The

Characteristics	Mean \pm S.D.		
	Group1	Group2	Group3
Age(years)	34.87 \pm 9.7	35.53 \pm 11.26	32.2 \pm 9.83
Weight(kg)	55.7 \pm 6.26	56.2 \pm 5.52	54.83 \pm 6.52
Sex	Males 16 Females 14	Males 18 Females 12	Males 16 Females 14

[Table/Fig-1]: Demographic Characteristics.



[Table/Fig-2]: Comparison of Mean Heart Rates in Groups 1, 2 & 3.



[Table/Fig-3]: Comparison of Systolic Blood Pressure in Groups 1, 2 & 3.

	Group 1	Group 2	Group 3
Onset of action	4.67 \pm 1.84	4.27 \pm 1.48	5.03 \pm 1.27
Duration of sensory block (min)	125 \pm 25.01*	228 \pm 39.86*	320 \pm 39.65*
Duration of motor block (min)	112.50 \pm 25.15*	198 \pm 50.2*	232 \pm 34.28*

[Table/Fig-4]: Characteristics of Sensory and Motor Block.
* p <0.01

intergroup comparison showed significant decrease in the systolic blood pressure of group 2 and group 3 from 25th minute to 60th minute as compared to group 1 as shown in [Table/Fig-3]. There was no significant difference noted in between group 2 and group 3. However, the incidence of hypotension requiring intervention was significantly more in group 2 as compared to group 1 and group 3. Other monitored parameters were comparable in all the groups throughout the study. No other untoward side effects were noticed in this study. The duration of sensory and motor block of the three groups are shown in [Table/Fig-4].

DISCUSSION

These results showed that the duration of sensory as well as motor block increased significantly in a dose dependent manner in groups in which clonidine was administered than in the control group. These findings support the observation made by Niemi et al., and Strebel et al., [7,8]. However, Benhamou and co-workers did not find prolongation of anaesthesia in their study [9], which in all probability must be due to the use of repeated boluses of intravenous fentanyl and epidural lignocaine whenever intraoperative analgesia was insufficient. This intervention may have lead to delay in regression of sensory blockade even in control group. Also, all the patients in the study were undergoing elective caesarean section that required consistently higher level of sensory blockade. Haemodynamically, heart rate was comparable in all the groups but as compared to its respective baseline value in group 3 and group 2, the heart rate decreased

significantly from 7th and 15th minute, respectively. This is explained by the fact that following intrathecal injection, clonidine is rapidly redistributed into plasma with a $t_{1/2}$ alpha of 7.3 minutes with peak arterial levels at 10 minutes and venous level within 30-45 minutes [10]. Clonidine after systemic absorption decreases heart rate by enhancing baseline vagal activity and by a direct action on the heart. Incidence of bradycardia was 2, 1 and 0 in group 1, group 2 and group 3, respectively. These findings coincide with that of De Negri et al., and BS Sethi et al., [11,12]. However, Niemi et al., reported a significant reduction in the heart rate [7]. That may be due to the greater dose of hyperbaric bupivacaine (15 mg) as well as clonidine (3 µg/kg). Systolic blood pressure in clonidine groups exhibited a decrease as compared to the control group. Similar trend was observed by Niemi et al., [7]. But the incidence of hypotension was more in groups 3 and 2 than group 1. Exact explanation could not be found but JC Eisenach reported increased haemodynamic stability with use of intermediate to large doses of clonidine in sheep that resulted in activation of both α_1 and α_2 receptors [13]. A detailed dose response study in humans may indicate a favourable intermediate dose. Haemodynamic derangement occurs in clonidine groups after 20 minutes as compared to control group and stabilizes near 60 minutes. NIBP monitoring for some more duration may clear the exact pattern of recovery to baseline values. Other side effects such as sedation and dry mouth were not found in this study as they were found in the study by Niemi et al., and BS Sethi et al., [7,12]. The former used diazepam per os to their patients on the morning of surgery and the latter used double the maximum dose of clonidine used in this study.

CONCLUSION

This study concludes that intrathecal clonidine as an adjuvant to bupivacaine is an effective and convenient method to prolong

spinal anaesthesia in a dose dependent manner for prolonged surgeries below the level of umbilicus with a limitation of close monitoring of NIBP and need of further studies with different doses to find the ideal dose of clonidine.

REFERENCES

- [1] McConachie I. Anaesthesia for the high risk patient. Cambridge: Cambridge University Press, 2002. 70-4.
- [2] Larson MD. History of Anaesthetic Practice. In: Miller RD. *Miller's Anaesthesia*. Sixth Edition. Philadelphia: Elsevier, 2005. 25-26.
- [3] Kestin L. A statistical approach to measure the competence of anaesthetic trainees at practical procedures. *Br J Anaesthesia*. 1995;75:805-09.
- [4] Tamsen A, Gordh T. Clonidine is not neurotoxic. *Lancet*. 1984;ii:876.
- [5] Filos KS, Goudas LC, Patroni O, Polyzou V. Haemodynamic and analgesic profile after intrathecal clonidine in humans: a dose response study. *Anesthesiology* 1994;81:591-601.
- [6] Dobrydjnov I, Axelsson K, Samarutel J, Holmstrom B. Postoperative pain relief following intrathecal bupivacaine combined with intrathecal or oral clonidine. *Acta Anaesthesiol Scand*. 2002;46:806-14.
- [7] 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;38:724-28.
- [8] Strebel S, Gurzeler JA, Schneider MC, Aechbach A, Kindler CH. Small dose intrathecal clonidine and isobaric bupivacaine for orthopedic surgery: a dose - response study. *Anesth Analg*. 2004;99(4):1231-38.
- [9] Benhamou D, Thorin D, Brichant JF, Dailland P, Milon D, Shneider M. Intrathecal clonidine and fentanyl with hyperbaric bupivacaine improves analgesia during cesarean section. *Anesth Analg*. 1998;87:609-13.
- [10] Eisenach JC, De Kock M, Klimscha W, et al. Alpha2-adrenergic agonists for Regional Anaesthesia: A Clinical Review of Clonidine (1984-1995). *Anesthesiology*. 1996;85:655-74.
- [11] De Negri P, Borelli F, Salvatore R, Visconti C, De Vivo P, Mastrorandi P. Spinal anaesthesia with clonidine and bupivacaine in young humans: interactions and effects on the cardiovascular system. *Minerva Anestesiol*. 1997;63(4):119-25.
- [12] Sethi BS, Samuel M, Sreevastava D. Efficacy of analgesic effects of low dose intrathecal clonidine as adjuvant to bupivacaine. *Indian Journal of Anaesthesia*. 2007;51(5):415-19.
- [13] Eisenach JC, Tong C. Site of haemodynamic effects of intrathecal α_2 -adrenergic agonists. *Anesthesiology*. 1991;74:766-71.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Neuroanaesthesia, MMIMSR, Mullana, Ambala, Haryana, India.
2. Assistant Professor, Department of Community Medicine, MMIMSR, Mullana, Ambala, Haryana, India.
3. Assistant Professor, Department of Anaesthesia, IGMC, Shimla, Himachal Pradesh, India.
4. Professor, Department of Anaesthesia, IGMC, Shimla, Himachal Pradesh, India.
5. Professor, Department of Anaesthesia, IGMC, Shimla, Himachal Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Ajay Wahi,
A-10, A Block, MMU Campus, Mullana, Ambala, Haryana-133207, India.
E-mail: ajaywahi81@yahoo.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Aug 19, 2015**

Date of Peer Review: **Oct 19, 2015**

Date of Acceptance: **Jan 09, 2016**

Date of Publishing: **Apr 01, 2016**