

# Effect of Intrathecal Clonidine on Post-operative Analgesia in Pregnant Patients Undergoing Lower Segment Caesarian Section

D Palaramkrishnan<sup>1</sup>, G Angel Vellut<sup>1</sup>, Heber Anandan<sup>2</sup>

<sup>1</sup>Assistant Professor, Department of Anesthesiology, Government Thoothukudi Medical College, Thoothukudi, Tamil Nadu, India, <sup>2</sup>Senior Clinical Scientist, Department of Clinical Research, Dr. Agarwal's Healthcare Limited, Tirunelveli, Tamil Nadu, India

## Abstract

**Introduction:** Neuraxial anesthesia is now the preferred technique for lower segment cesarean sections (LSCS). Although epidural, spinal, continuous spinal, and combined spinal-epidural techniques have all been advocated, the most cesarean sections are performed under single-shot spinal anesthesia.

**Aim:** To evaluate the efficacy of clonidine in prolonging the duration of post-operative analgesia when combined with bupivacaine and the property of clonidine to potentiate the analgesic effect of bupivacaine and to observe the safety of intrathecally administered clonidine.

**Materials and Methods:** Pregnant patients belonging to the American Society of Anesthesiologists Physical Status I and II from 18 to 28 years, weighing 45-70 kg were included in the study. The patients were randomly allocated into two groups, Group B and Group C. Group B administered with 0.5% hyperbaric bupivacaine 10 mg and Group C administered with 0.5% hyperbaric bupivacaine 10 mg with clonidine 75 µg.

**Results:** A mean duration of analgesia in Group B is  $176.9 \pm 69.5$  and Group C is  $288.6 \pm 130.3$ . Time to 2 segment regression in Group B is  $126.8 \pm 56.5$  and Group C is  $214.6 \pm 103.5$ .

**Conclusion:** An addition of 75 µg of clonidine to hyperbaric bupivacaine is safe and beneficial to pregnant patients posted for LSCS.

**Key words:** Analgesic, Bupivacaine, Clonidine, Lower segment caesarean sections

## INTRODUCTION

Bupivacaine in orthopedic surgeries had proved that the combination of clonidine was effective in preventing the tourniquet pain and effectively prolonging the post-operative analgesia. Spinal anesthesia has increasingly become the technique of choice for lower segment cesarian section.<sup>1</sup> It has the advantages of simplicity of technique,<sup>2,3</sup> rapid onset of action, and reliability in producing uniform sensory and motor blockade as compared to epidural anesthesia.<sup>4-6</sup> Its main disadvantage relates to its limited

duration of action and hence the lack of long-lasting post-operative analgesia. Spinal anesthesia and post-operative analgesia can be prolonged using adjuvant to local anesthetic such as adrenaline,<sup>7</sup> midazolam,<sup>8</sup> opioids, neostigmine, and clonidine.<sup>9-14</sup> Clinical studies have suggested that intrathecal clonidine prolongs sensory as well as a motor block of spinal anesthesia. It decreases local anesthetic requirements and provides prolonged post-operative analgesia.<sup>9,14-17</sup> Other beneficial effects are anti-emesis, reduced post spinal shivering, anxiolysis, and sedation.<sup>18</sup> Increased sedation caused by it may also be unwanted at times. The necessity to find out the lower effective dose of clonidine to avoid its known side effects like hypotension and bradycardia and sedation prompted us to design this study.

### Aim

To evaluate the efficacy of clonidine in prolonging the duration of post-operative analgesia when combined with

### Access this article online



www.ijss-sn.com

Month of Submission : 08-2016  
Month of Peer Review : 08-2016  
Month of Acceptance : 09-2016  
Month of Publishing : 10-2016

**Corresponding Author:** Heber Anandan, No. 10, South By-pass Road, Vannarpettai, Tirunelveli - 627 003, Tamil Nadu, India.  
Phone: +91-9894067910. E-mail: clinicalresearch@dragarwal.com

bupivacaine and the property of clonidine to potentiate the analgesic effect of Bupivacaine and to observe the safety of intrathecally administered clonidine.

## MATERIALS AND METHODS

Open-labeled, randomized controlled study was conducted in Department of Anesthesiology, Tirunelveli Medical College in Pregnant patients belonging to American Society of Anesthesiologists Physical Status I and II. Patients from 18 to 28 years, weighing 45-70 kg were included in the study. Patients with systemic illness, patients with partial block or failed block, height <145 cm, procedures ending with hysterectomy or requiring blood transfusion, anemia, bleeding disorders, contraindication to clonidine, patients with psychiatric problems, and patients having spinal deformities were excluded from the study. After getting, informed consent, the patients were randomly allocated into two groups. Group “B” was administered with bupivacaine and Group “C” was administered with clonidine group. 0.5% hyperbaric bupivacaine 10 mg was injected in Group B and 0.5% hyperbaric bupivacaine 10 mg with clonidine 75 µg was injected in Group C.

## RESULTS

The study was conducted on 70 patients randomly allotted into 2 groups as given below and the visual analog pain scale assessed.

After 2 h postoperatively, both Groups B and C patients exhibited a pain score of 0-1 and were comfortable, manifesting no signs of pain (Table 1). After 3 h, 8 patients in Group B manifested mild to moderate levels of pain requiring systemic analgesic supplementation. In Group C, only 5 patients manifested pain which required analgesic supplementation (Table 2). After 4 h, 31 patients in Group B manifested pain requiring systemic analgesic supplementation. In Group C, only 8 patients manifested pain which required analgesic supplementation (Table 3). After 6 h, 34 patients in Group B manifested pain, with almost 97% requiring systemic analgesic supplementation (Table 4).

In Group C, only 23 patients manifested pain, with an average only 66% required analgesic supplementation. 12 of the patients did not show any sign of pain, which is 34% of the study group had a good analgesic effect even after 6 h duration.

The mean “duration of analgesia” and mean “time to 2 segment regression” between the two groups were

**Table 1: VAP score (2<sup>nd</sup> h)**

Pain score	Number of patients (%)	
	Group B	Group C
0-1	35 (100)	35 (100)
2-4	0 (0)	0 (0)
5-6	0 (0)	0 (0)
>7	0 (0)	0 (0)

VAP: Visual analog pain scale

**Table 2: VAP score (3<sup>rd</sup> h)**

Pain score	Number of patients (%)	
	Group B	Group C
0-1	7 (20)	21 (60)
2-4	20 (57)	9 (26)
5-6	6 (17)	5 (14)
>7	2 (6)	0 (0)

VAP: Visual analog pain scale

**Table 3: VAP score (4<sup>th</sup> h)**

Pain score	Number of patients (%)	
	Group B	Group C
0-1	3 (8)	20 (57)
2-4	1 (3)	7 (20)
5-6	6 (17)	6 (17)
>7	25 (72)	2 (6)

VAP: Visual analog pain scale

**Table 4: VAP score (6<sup>th</sup> h)**

Pain score	Number of patients (%)	
	Group B	Group C
0-1	0 (0)	6 (17)
2-4	1 (3)	6 (17)
5-6	4 (12)	10 (30)
>7	30 (85)	13 (36)

VAP: Visual analog pain scale

statistically significant ( $P < 0.0001$ ) (Table 5). The hemodynamic variables such as mean arterial pressure (MAP), pulse rate did not significantly differ at all the time periods of monitoring (5, 10, 15, 20, 30, 60, 90, 120). The SPO<sub>2</sub> of Group B was lesser than Group C at 5<sup>th</sup> min only. In all other time periods, the SPO<sub>2</sub> of the Group C was lesser than Group B which is statistically significant, though it is not clinically significant.

## DISCUSSION

Clonidine added to bupivacaine for spinal anesthesia in caesarean section improves the immediate post-operative analgesia effect. The effective dose range of intrathecal clonidine for post-op analgesia is not known till date. Actually, all effects of clonidine including

**Table 5: Comparison of duration of analgesia**

Category	n	Mean±SD		Mean difference	t	Diff	Significance
		Group B	Group C				
Duration of analgesia	35	176.9±69.5	288.6±130.3	111.7	4.475	68	P<0.0001
Time to 2 segment regression	35	126.8±56.5	214.6±103.5	87.8	3.955	68	P<0.0001

SD: Standard deviation

analgesia are dose dependent. This study suggests that compared to bupivacaine alone, the addition of 75 µg clonidine to bupivacaine produced a strong analgesia with a mean duration of 288 minutes. Furthermore, our patients were not administered any additional opioids or tranquilizers perioperatively that may have potentiated the analgesic action of clonidine. Van Essen *et al.*<sup>19</sup> studied the effect of addition of intrathecal clonidine to hyperbaric bupivacaine on post-operative pain and morphine requirements after caesarean section. He demonstrated that addition of 75 µg clonidine to hyperbaric bupivacaine prolongs spinal analgesia and the motor block after caesarean section and improves early analgesia. In this study using clonidine 75 µg alone the analgesia lasted for a mean of 288 min. The dose is lesser than that used by Coombs *et al.*, but the duration of analgesia is closer to that study even without opioid. Mendez *et al.*<sup>13</sup> used epidural clonidine in doses of 400 and 800 µg for cesarean section, and they found that 800 µg group had 5 h of median duration of analgesia and this is closer to this study. This study shows that the intrathecal route required lesser dose than epidural route but with the same duration of analgesia and is safer with no side effects. Filos *et al.*<sup>20</sup> 150, 300, 450 µg intrathecal clonidine for its hemodynamic effects. They found the 300 and 450 µg group had hemodynamic stability, but the 150 µg group presented with immediate fall in MAP but with no delayed fall in this group. There was no incidence of significant bradycardia in all the three groups. This study with 75 µg clonidine also showed no significant hemodynamic changes. Moreover, it had no measurable deleterious side-effects in mother. Although MAP was lower in the Group C, this apparently was not considered clinically important, as the fall in MAP was manageable with intravenous fluids and the occurrence of bradycardia was not significantly different between the two groups. Furthermore, the average MAP did not decrease >20% from baseline.

## CONCLUSION

This study has demonstrated that addition of 75 µg clonidine to hyperbaric bupivacaine prolongs post-operative analgesia and the two segment regression after caesarean section, without clinically significant

hemodynamic derangements or any adverse effects. Hence, intrathecal clonidine along with bupivacaine proves to be a safer alternative to intrathecal opioids and with a dose of 75 µg, the hemodynamic profile is also very acceptable. Thus, intrathecal clonidine 75 µg not only potentiates and prolongs the analgesic effect of bupivacaine but also has a good safety profile for intrathecal use.

## REFERENCES

1. Tamsen A, Gordh T. Clonidine is not neurotoxic. *Lancet* 1984;2:876.
2. Tamsen A, Gordh T. Epidural clonidine produces analgesia. *Lancet* 1984;2:231-2.
3. Gordh T Jr, Feuk U, Norlén K. Effect of epidural clonidine on spinal cord blood flow and regional and central hemodynamics in pigs. *Anesth Analg* 1986;65:1312-8.
4. Eisenach JC, Grice SC. Epidural clonidine does not decrease blood pressure or spinal cord blood flow in awake sheep. *Anesthesiology* 1988;68:335-40.
5. Crosby G, Russo MA, Szabo MD, Davies KR. Subarachnoid clonidine reduces spinal cord blood flow and glucose utilization in conscious rats. *Anesthesiology* 1990;73:1179-85.
6. Eisenach JC, Dewan DM, Rose JC, Angelo JM. Epidural clonidine produces antinociception, but not hypotension, in sheep. *Anesthesiology* 1987;66:496-501.
7. Gordh T Jr, Post C, Olsson Y. Evaluation of the toxicity of subarachnoid clonidine, guanfacine, and a substance P-antagonist on rat spinal cord and nerve roots: Light and electron microscopic observations after chronic intrathecal administration. *Anesth Analg* 1986;65:1303-11.
8. Yaksh TL, Rathbun M, Jage J, Mirzai T, Grafe M, Hiles RA. Pharmacology and toxicology of chronically infused epidural clonidine.HCl in dogs. *Fundam Appl Toxicol* 1994;23:319-35.
9. Unnerstall JR, Kopajtic TA, Kuhar MJ. Distribution of alpha 2 agonist binding sites in the rat and human central nervous system: Analysis of some functional, anatomic correlates of the pharmacologic effects of clonidine and related adrenergic agents. *Brain Res* 1984;319:69-101.
10. Butterworth J, Strichartz G. Differential nerve block by the a2 adrenergic receptor agonists clonidine and guanfacine. *Anesthesiology* 1992;77 Suppl:A861.
11. Gaumann DM, Brunet PC, Jirounek P. Hyperpolarizing afterpotentials in C fibers and local anesthetic effects of clonidine and lidocaine. *Pharmacology* 1994;48:21-9.
12. Eisenach J, Detweiler D, Hood D. Hemodynamic and analgesic actions of epidurally administered clonidine. *Anesthesiology* 1993;78:277-87.
13. Mendez R, Eisenach JC, Kashtan K. Epidural clonidine analgesia after cesarean section. *Anesthesiology* 1990;73:848-52.
14. Eisenach JC, Lysak SZ, Viscomi CM. Epidural clonidine analgesia following surgery: Phase I. *Anesthesiology* 1989;71:640-6.
15. Bonnet F, Boico O, Rostaing S, Loriferne JF, Saada M. Clonidine-induced analgesia in postoperative patients: Epidural versus intramuscular administration. *Anesthesiology* 1990;72:423-7.
16. Filos KS, Goudas LC, Patroni O, Polyzou V. Intrathecal clonidine as a sole analgesic for pain relief after cesarean section. *Anesthesiology* 1992;77:267-74.

17. De Kock M, Crochet B, Morimont C, Scholtes JL. Intravenous or epidural clonidine for intra- and postoperative analgesia. *Anesthesiology* 1993;79:525-31.
18. Bernard JM, Kick O, Bonnet F. Comparison of intravenous and epidural clonidine for postoperative patient-controlled analgesia. *Anesth Analg* 1995;81:706-12.
19. Van Essen EJ, Bovill JG, Ploeger EJ, Schout BC. A comparison of epidural clonidine and morphine for postoperative analgesia. *Eur J Anaesth* 1990;7:211-8.
20. Filos KS, Goudas LC, Patroni O, Polyzou V. Hemodynamic and analgesic profile after intrathecal clonidine in humans. A dose-response study. *Anesthesiology* 1994;81:591-601.

**How to cite this article:** Palaramakrishnan D, Vellut GA, Anandan H. Effect of Intrathecal Clonidine on Post-operative Analgesia in Pregnant Patients Undergoing Lower Segment Caesarian Section. *Int J Sci Stud* 2016;4(7):127-130.

**Source of Support:** Nil, **Conflict of Interest:** None declared.