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ORIGINAL ARTICLE

Effect of low dose intrathecal clonidine as an adjuvant to hyperbaric bupivacaine on postoperative analgesia in patients undergoing elective infra umbilical surgeries

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ABSTRACT

Background: Clonidine, an imidazole derivative with α-2 adrenergic agonist action, when used intrathecally gives good analgesia and is claimed to have minimal side effects as compared to opioids1. We evaluated the effects of low dose intrathecal clonidine as an adjuvant to hyperbaric bupivacaine on postoperative analgesia in patients undergoing elective infraumbilical surgeries.

Methodology: In a prospective, double blind, randomized controlled study, 60 patients undergoing elective infraumblical surgeries were randomly divided into two groups of 30 each. Group 1 received 15 mg of 0.5% hyperbaric bupivacaine with 0.5 µg/kg clonidine and Group 2 received 15 mg of 0.5% hyperbaric bupivacaine with normal saline (same volume). The onset of sensory block, duration of motor blockade, VAS score and time for first rescue analgesia were noted. Patients were monitored for any side effects.

Results: Demographic profile of the patients were similar in both the groups. Group 1 had faster onset of sensory blockade ($p < 0.001$) as compared to Group 2. Mean time for 2 segment sensory level regression was delayed in Group 1. Group 1 noted a prolongation in duration of analgesia i.e., 165.43 ± 23.13 min as compared to Group 2 where rescue analgesia was demanded earlier.

Conclusion: Intrathecal clonidine in a dose of 0.5 µg/kg shortens the onset of sensory blockade, increases the duration of sensory blockade and complete motor recovery. Duration of postoperative analgesia is significantly prolonged and the time for requirement of rescue analgesia is prolonged without causing significant side effects if clonidine is used in low doses.

Key words: Intrathecal; Clonidine; Bupivacaine; Surgeries, Infraumbilical

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INTRODUCTION

Central neuraxial opioids, intrathecal as well as epidural, offer perceived benefit of selective analgesia without effect on sensory or motor blockade. However, side effects such as potentially catastrophic delayed respiratory depression, pruritus, urinary retention have prompted further research to develop non-opioid analgesic with less worrisome side effects.[1,2] Clonidine an imidazole derivative, α 2 receptor agonist, prolongs the duration of intrathecally administrated local anesthetic drug and has potent antinociceptive properties. Clonidine is known to increase both sensory and motor blockade of LA.[3] The analgesic effect following its intrathecal administration is mediated spinally through activation of post synaptic α 2 receptors in substantia gelatinosa of spinal cord.[4,5] Many studies have described the use of intrathecal clonidine in wide range (15-150 μg)[6-9] and have reported side effects as bradycardia, sedation and hypotension needing intervention.[10,11] We planned to study the efficacy of intrathecal clonidine 0.5 μg/kg for elective infra umbilical surgeries to note if the benefits of clonidine as an adjuvant outweigh the side effects.

METHODOLOGY

After the hospital ethical committee approval, a written, informed, signed consent of the patients was duly obtained. A prospective, randomised, double blind, comparative study was carried out. A total of 60 patients belonging to ASA physical status I or II scheduled to undergo elective arthroscopy and ACL repair surgeries, lower abdominal surgeries as hernia, gynaecology surgeries like vaginal hysterectomy, total abdominal hysterectomy were enrolled in this study. The patients with cardiovascular disease on psychiatric drugs, hypersensitivity to Clonidine or LA, and all known contraindications for subarachnoid block were excluded from the study. They were randomly divided in 2 groups of 30 each: Group 1 (30) who received intrathecal 0.5% heavy bupivacaine (15 mg) with clonidine 0.5 μg/kg and Group 2 (30) received intrathecal 0.5% heavy bupivacaine (15 mg) with normal saline (same volume). The groups were allocated using sealed envelopes. Every patient was made to understand linear visual analogue scale (VAS) (denoting 0 = no pain and 10 = worst imaginable pain) preoperatively.[12]

Under all aseptic precautions, subarachnoid block was performed in the sitting position using a 25G Quincke needle and the subarachnoid space was entered at the L3-L4 level. Immediately after the subarachnoid injection, patient was made supine. Intra operatively, no sedation or analgesia was given to any of the patients. All patients were monitored peri-operatively for pain using VAS score. Intravenous diclofenac sodium 75 mg was used as rescue analgesia at VAS score of 3 or more. Pre-spinal hemodynamics (baseline heart rate, BP), intraoperatively at 5, 10, 15, 30, 60, 120, 180, 240 and 360 min and post-operatively up to 24 h were noted. Onset of sensory analgesia taken as loss of pin-prick sensation at dorsum of foot. Degree of motor block was assessed by modified Bromage scale.[13] Two segment dermatomal regression level of sensory block from T10 level was noted. Time of demand of first request analgesia was noted. Total duration of post-operative analgesia, duration of effective analgesia (time taken from the start of spinal anesthesia up to the requirement time of first rescue analgesia) was noted. Sedation was assessed by Ramsay sedation score. Any adverse effects were noted. Analgesia in the post-operative period was assessed by VAS. Sedation was assessed at 3, 4, 5, 6, 8, and 12 h. Data were obtained and statistical analysis was done using paired t-test, unpaired t test and two sample proportion test and Mann-Whitney U test for sedation.

RESULTS

The demographic data of the two groups were comparable with respect to age, weight, height, gender and duration of surgery (Table 1).

Haemodynamic parameters recorded showed fall in mean heart rate in Group C from 30 min to the end of 360 min (Figure 1). The decrease from baseline value within the Clonidine group was also statistically significant from 30 min to the end of 360 min ($p < 0.001$), (Table 2) but none of the patients required atropine, this decrease in heart rate was not seen in the Saline group. There was significant drop in systolic and diastolic

Table 1: Demographic data in both groups [Mean ± SD]

Demographic parameters	Group 1 (n=30)	Group 2 (n=30)	p value
Age (yrs)	39.33 ± 9.40	37.73 ± 9.75	0.52
Weight (kg)	61.63 ± 9.89	59.67 ± 5.99	0.356
Height (cm)	153.93 ± 12.66	151.90 ± 18.86	0.625
Gender (M/F)*	19:11	24:6	0.382
Duration of surgery (min)	176.33 ± 41.33	164.33 ± 32.21	0.215

*n

clonidine as an adjuvant to intrathecal bupivacaine

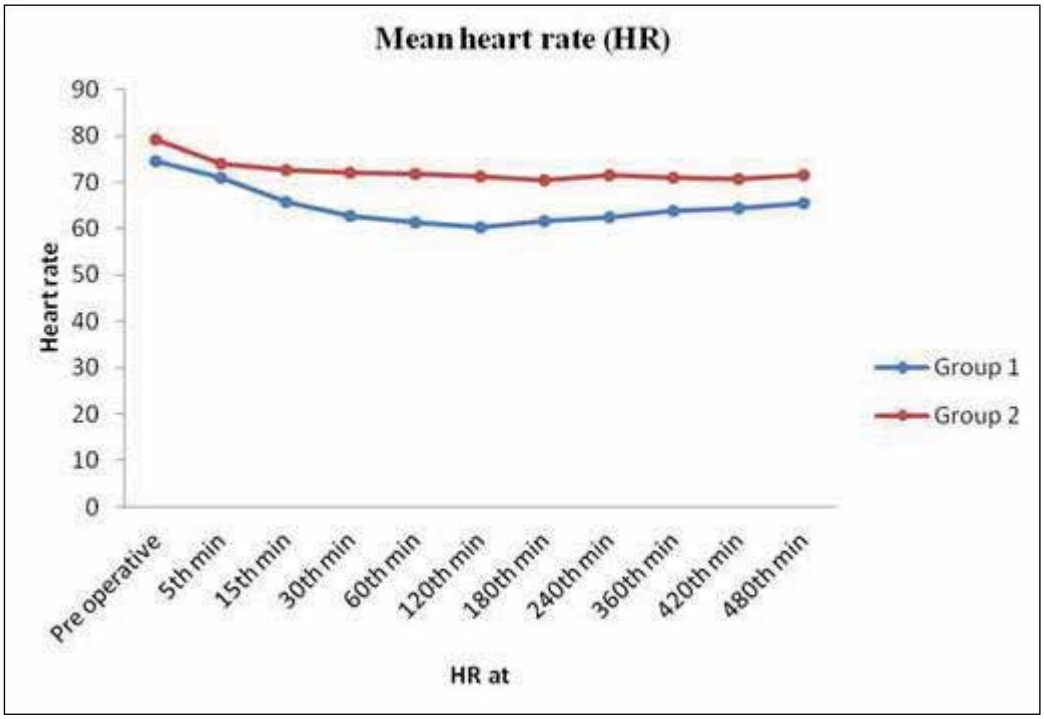

Figure 1: Mean Heart rate at different time intervals.

Table 2: Assessment of heart rate, systolic and diastolic blood pressure over 24 hours

Time (min)	Heart rate (bpm) (Mean ± SD)			Systolic BP (mmHg) (Mean ± SD)			Diastolic BP (mmHg) (Mean ± SD)		
	Group 1 (n=3)	Group 2 (n=30)	p-value	Group 1 (n=30)	Group 2 (n =30)	p-value	Group 1 (n=30)	Group2 (n=30)	p-value
Pre-operative	74.63 ± 7.98	79.13 ± 11.13	0.078	128.27 ± 13.45	127.60 ± 10.36	0.83	77.80 ± 11.49	75.93 ± 11.42	0.53
5	70.87 ± 8.62	74.03 ± 8.90	0.176	122.47 ± 8.64	106.80 ± 10.29	<0.001	74.33 ± 10.43	65.90 ± 11.62	0.004
15	65.83 ± 8.20	72.67 ± 8.76	0.003	118.53 ± 7.77	101.27 ± 10.25	<0.001	71.60 ± 9.98	59.63 ± 10.04	<0.001
30	62.73 ± 7.66	72.00 ± 8.40	< 0.001	114.23 ± 7.85	100.40 ± 9.78	<0.001	68.33 ± 9.46	54.40 ± 9.09	<0.001
60	61.27 ± 7.66	71.83 ± 8.81	< 0.001	110.27 ± 8.50	103.73 ± 9.75	0.008	64.80 ± 9.12	54.33 ± 7.47	<0.001
120	60.20 ± 7.51	71.30 ± 8.33	< 0.001	108.20 ± 8.52	107.13 ± 9.57	0.65	62.40 ± 8.86	58.20 ± 7.21	0.049
180	61.73 ± 8.89	70.30 ± 8.73	< 0.001	108.17 ± 7.74	112.57 ± 8.47	0.04	60.30 ± 8.61	61.93 ± 8.20	0.455
240	62.33 ± 9.00	71.50 ± 9.26	< 0.001	110.73 ± 9.46	114.73 ± 6.90	0.67	60.00 ± 8.44	64.33 ± 7.59	0.041
360	63.93 ± 6.53	71.03 ± 8.83	0.001	118.97 ± 8.98	118.27 ± 7.87	0.749	64.67 ± 10.76	66.33 ± 9.10	0.52
420	64.30 ± 7.01	70.70 ± 8.56	0.002	122.07 ± 10.20	121.00 ± 8.55	0.662	69.13 ± 11.10	68.47 ± 9.12	0.8
480	65.43 ± 6.96	79.13 ± 11.13	0.005	125.07 ± 11.49	122.53 ± 9.29	0.352	72.67 ± 12.70	69.07 ± 10.11	0.23

Table 3: Duration of onset of sensory block, duration of motor block and analgesia

Parameters	Group 1	Group 2	p- value
Onset sensory (min)	1.20 ± 0.24	3.88 ± 0.55	< 0.001
Duration of motor (min)	234.00 ± 29.9	178.17 ± 23.76	< 0.001
Duration of analgesia (min)	376.33 ± 37.71	205.07 ± 28.08	< 0.001

blood pressure noted in both the groups (Table 2).

There was significant difference between both groups with respect to onset of sensory blockade (Table 3). It was observed that patients in group 1 (1.20 ± 0.24 min) had faster onset of sensory block as compared to those in Group 2 (3.88 ± 0.55 min). The duration of motor blockade was significantly longer in Clonidine group as compared to Saline group. The mean time for two segment regression from T10 for both the groups was delayed in Group 1 (183 ± 5.97) as compared to Group 2 (92.10 ± 5.70) .The duration of analgesia was prolonged in Clonidine Group.

There is significant difference between Group 1 and Group 2 with respect to demand of rescue analgesia (min) $p < 0.05$. Patients in Group 1 (376.33 ± 37.7 min) requested for rescue analgesia later as compare to patients in Group 2 (205.07 ± 28.08 min). Patients in Group 1 were pain free for longer duration as compared to Group 2. There was no significant difference in sedation score in both the groups (Figure 2).

DISCUSSION

Pain relief after surgery is an important and essential part of post-operative care to aid early rehabilitation. Methods to prolong analgesia and improve its quality with minimal side effects have always been sought. Many workers have attempted to prolong the effect of hyperbaric bupivacaine spinal anesthesia and provide postoperative analgesia with the use of adjuvant drugs.[14]

Opioids which are commonly used as an adjuvant for spinal anesthesia are not devoid of side effects such as pruritus, somnolence, nausea, vomiting or respiratory depression.[15,16]

In our study, we used low doses of clonidine as an adjuvant to intrathecal bupivacaine for subarachnoid block, aiming to have effective low dose of clonidine with minimal side effects. Our primary outcome was duration of analgesia extending to postoperative period (time to first dose of postop rescue analgesia).

In our study, average onset time of sensory blockade was 1.2 min in the clonidine group (Group 1) which was significantly shorter than the control group (Group 2) with average onset time of 3.88 min.

The motor blockade and duration of analgesia in

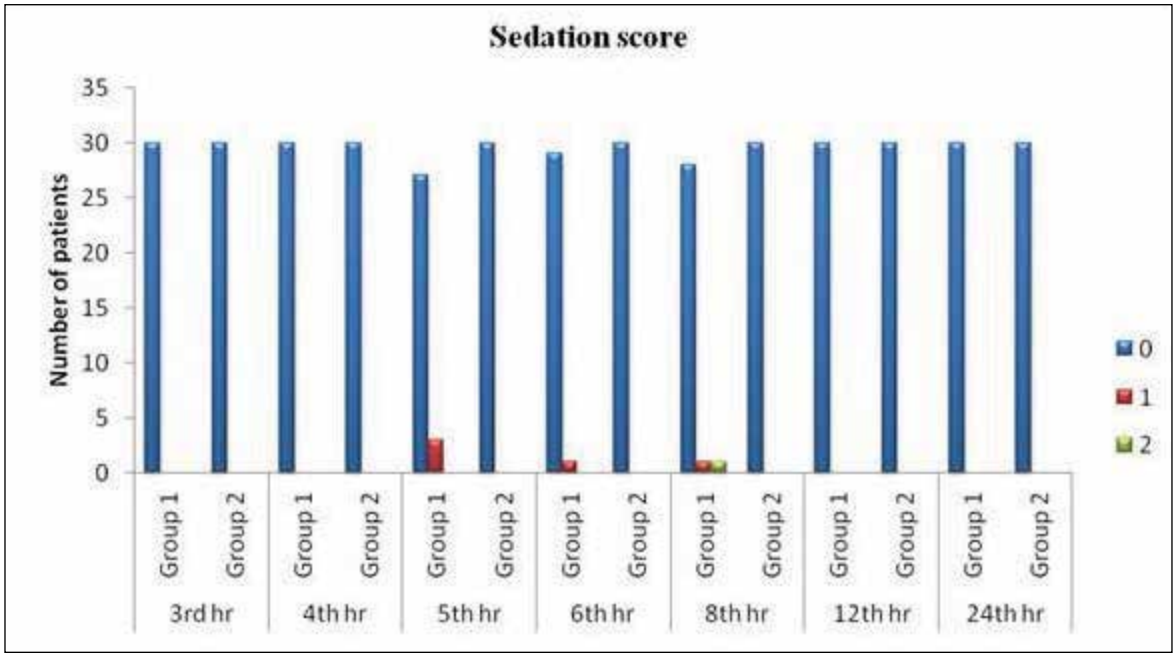

Figure 2: Sedation score

clonidine group lasted for 234 min (3.9 h) and 376 min (6.2 h) respectively, comparable to the duration observed in the study by Bhar et al. (who used 30 μg clonidine in abdominal hysterectomy) and observed 224 min (3.73 h) and 314 min (5.23 h) respectively.[17]

B.S. Sethi et al. studied effect of low dose intrathecal clonidine i.e. 1 μg/kg with max dose 70 μg with hyperbaric 0.5% bupivacaine (12.5 ml) for gynaecological surgeries.[1] The duration of subarachnoid block in their study was 218 (150-240) min and duration of effective analgesia was 614 (480-1140) min and side effects of sedation, pruritus and nausea were less. The longer duration of analgesia is proportionate to the dose of clonidine but was be limited by side effects, although few.

In our study, patients in clonidine group (Group 1) requested for rescue analgesia significantly later (376.33 ± 37.7 min) as compared to patients with saline group (Group 2)(205.07 ± 28.08 min). The duration of analgesia was prolonged in clonidine group in our study (376.33 ± 37.71) compared to control group ($p < 0.001$), which is significant.

Grandhe et al. studied unilateral lower limb orthopaedic surgeries with intrathecal clonidine in doses 1 μg/kg and 1.5 μg/kg.[16] They found prolonged sensory analgesia upto 6.3 ± 0.8 h with 1 μg /kg clonidine group and 7.3 ± 0.9 h in 1.5 μg/kg clonidine group with significantly reduced requirement of rescue analgesia. Incidence of hypotension was 67% and 53% respectively. They noticed no significant sedation or adverse hemodynamic effects in any patient.[8]

The data obtained from our study indicates that clonidine 0.5 μg/kg added to 0.5% hyperbaric bupivacaine (15 mg) prolongs the duration of subarachnoid block and prolongs the duration of analgesia and thus reduces the postoperative analgesic requirement. Results obtained from our study about onset of sensory blockade, duration of motor analgesia, rescue analgesia and side effects are comparable to above studies.

Stephen et al. in dose responsive study using intrathecal clonidine 37.5 μg (Group 1), 75 μg (Group 2), and 150 μg (Group 3) with isobaric 0.5% bupivacaine 18 mg in patients scheduled for knee or hip arthroplasties. Duration of subarachnoid block in Group 1 was 288 ± 62 min, 311 ± 101 min and 337 ± 78 min in Group 2 and 3 respectively.[18]

Clonidine decreases HR by a presynaptic mediated inhibition of nor epinephrine release and by a direct depression of atrioventricular nodal conduction after systemic absorption. In the present study, clonidine group showed a fall in heart rate from baseline while in the saline group, no significant change in heart rate was seen.

Unlike the earlier studies, none of the patient in our study had significant sedation which confirms the findings of Grandhe et al. Sethi et al. which explains that the sedative effect of clonidine is dose dependant and thus explains the absence of sedative effects in our study. Dryness of mouth atypical side effect of clonidine was reported by two patients.

CONCLUSION

Low dose intrathecal clonidine 0.5 μg/kg with bupivacaine hastens the sensory onset of block, increases the duration of motor blockade and prolongs the duration of analgesia with minimal side effects in infraumbilical surgeries. Prolonged duration of analgesia with clonidine allows reduced use of opioids, other adjuvants with no serious side effect.

Conflict of interest: None declared by the authors

Authors' contribution:

PS – Concept, conduct of study, manuscript preparation

AM – manuscript writing, literature review

ND, RP – Manuscript editing

DNA - literature review

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