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Original Research Article

Effect of Clonidine and Bupivacaine in Intrathecal Versus Peripheral Nerve Block Routes in Arthroscopic Knee Surgery: Prospective Observational Study

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Abstract

Background and Aims: A large number of patients undergoing arthroscopic knee surgeries complain of inadequate pain relief. Clonidine and bupivacaine were administered through intrathecal route and femorosciatic nerve block route and evaluated for more favourable perioperative outcome between them.

Methods: An open label randomized controlled trial was planned in a tertiary care hospital in Eastern India in which 50 American Society of Anaesthesiologists I and II patients undergoing arthroscopic knee surgery were enrolled. They were divided into two groups-Group IT and Group NB, by using computer-generated block randomization technique. Group IT received 1 µg/kg of clonidine along with 0.5% hyperbaric bupivacaine, whereas Group NB received 0.25% bupivacaine and 1 µg/kg clonidine in femorosciatic nerve block (FSNB). Postoperative pain-free interval and block characteristics were the primary outcomes studied.

Results: Pain-free duration was 522.08(±21.18) min in Group NB ($P < 0.001$) in comparison to 325.33(±17.85) min in Group IT. Sensory block and motor blockade in NB were 469.58(± 15.17) and 264.88(±14.87) min, respectively, and was significantly prolonged in comparison to Group IT ($P < 0.001$). The mean rescue analgesic requirement was less in Group NB as compared to Group IT.

Conclusion: Clonidine in a dose of 1 µg/kg with bupivacaine has better perioperative outcome through FSNB route in comparison to its use via intrathecal route in arthroscopic knee surgery. It provided stable haemodynamic and respiratory parameters intra and postoperatively, increased duration of sensory block and pain-free period, lesser 24 h rescue analgesic requirement making it ideal for post knee surgery pain.

Keywords: Arthroscopic Surgery, Clonidine, Postoperative Pain.

Introduction

Increased performance of arthroscopic knee surgeries necessitates adequate postoperative analgesia.[1] Regional anaesthetic techniques with adjuvants are commonly utilized to extend the analgesic effect into the postoperative period.[2] Clonidine, an α2-adrenergic receptor agonist, has been evaluated as an alternative to intrathecal opioid for control of pain and has proven to be a potent analgesic, free of at least some of the opioid-related side effects.[3] On the other hand, clonidine has also been shown to prolong sensory analgesia when given as an adjunct to peripheral nerve blocks, with lesser episodes of hypotension and bradycardia.[4] Although the studies employing clonidine show a prolongation in the analgesic duration, different times and dosages have been used with limited studies showing comparison between the efficacies when used through different routes in similar doses in a single type of surgery.[2] The present study has been planned to explore the effect of clonidine with bupivacaine through two different routes- intrathecal and peripheral nerve blocks (femoral-sciatic nerve block in this case) and evaluate more favourable outcome between the two. Primary outcome of interest will be analgesic duration and block characteristics while the secondary outcomes will be hemodynamic and sedation scores.[2]

Methods

After approval from Institutional Ethics Committee and written informed consent, 50 American Society of Anaesthesiologists I and II patients of either sex undergoing arthroscopic knee surgery were included in this open label randomized controlled trial. Patients between 20 and 40 years of age and weighing between 60 and 75 kg were enrolled. Any patients with contraindications to spinal anaesthesia like spinal deformities, neurological disease, coagulation abnormalities, any local infections at the site of injection, and refusal to give consent were excluded from the study. Patients with a history of drug allergy or contraindications to nonsteroidal anti-inflammatory drugs were also excluded from the study.[2] Randomization was done by computer generated block randomization procedure. The patients were randomly allocated to either of the two routes of anaesthesia; those given bupivacaine and clonidine intrathecally designated as Group IT, and those given bupivacaine and clonidine through FSNB as Group NB. No blinding was possible in this study. No narcotics were used in premedication.[2]

Patients in Group IT received spinal anaesthesia with hyperbaric bupivacaine (0.5%)-2 ml and clonidine (1 µg/kg) followed by tilting of the table towards the side of operating leg (unilateral spinal anaesthesia). The level of spinal anaesthesia was ensured to be above the T11 dermatome. On the other hand, Group NB patients received 20 ml and 30 ml of isobaric bupivacaine (0.25%) along with 0.5 µg/kg clonidine in each of the femoral and sciatic nerve block respectively. The nerve block was performed with the help of nerve stimulator (Plexygon, Vygon, Ecouen, France). With an initial current of 1 mA and frequency of 1 Hz, the nerve stimulator needle was introduced till the motor response was present at a current of approximately 0.5mA, following which local anaesthetic mixture was administered.[5] The onset of block in each patient was recorded. Sensory block was tested by loss of cold temperature and pin prick sensation around knee. Motor blockade was measured by modified Bromage scale[6], considering Stage 2 as satisfactory for the surgery to proceed.

Modified Bromage Scale[6]:

0: No motor block
1: Inability to raise extended leg; able to move knees and feet
2: Inability to raise extended leg and move knee; able to move feet 3: Complete block of motor limb

Hemodynamic and respiratory parameters (Pulse rate, NIBP, respiratory rate, SpO2) was monitored every 5 min up to 30 min after giving anaesthesia and thereafter every 15 min intraoperatively and 30 min postoperatively for 4 h. Thereafter, patients were monitored postoperatively for duration of sensory and motor block.

While studying block characteristics, return of sensation around the knee joint and return of motor power at the knee joint was tested at 15 min interval in the postoperative period. The duration of sensory block was defined from injection of the drug till return of sensation around the knee joint (L4 dermatome).[2] Modified Bromage scale was used to measure motor block.[6] The duration of motor block was defined from injection of the test drug up to the ability to flex knee joint (modified Bromage scale - Stage 1).

Patients were educated about the 11 point verbal rating score (VRS) where 0 as no pain and 10 as worst imaginable pain.[2] When the VRS was more than 3 at any point of time within 24 h postoperatively, first rescue analgesia in the form of diclofenac 75 mg IM was given. If the VRS after 30 min of administration of IM diclofenac was greater than 3, another dose of IM diclofenac was administered till a total of 3 doses in 24 h. If the pain score at any time in the 24h was more than 3 even after 3 doses of first rescue analgesia, a second rescue analgesic of IV fentanyl of 1 µg/kg was administered. The total rescue analgesic consumption in 24 h in each group were noted. Sedation was assessed with Ramsay sedation scores both intra- and post-operatively at 15- and 30-min intervals respectively till sedation scores achieved baseline values. All patients were shifted to the wards for 24 h observation. Sample size estimation was based on a previous study where the response within each subject group was normally distributed with standard deviation 2.[7] If the true difference between each group is 2, we needed to study 22 subjects of the Group IT and 22 subjects of the Group NB to be able to reject the null hypothesis that the population means of both the groups are equal with probability (power) 0.9. The Type I error probability associated with this test of this null hypothesis is 0.05. Therefore, we ensured at least 25 patients in each group to adjust for any potential dropouts. Levene's test was used to assess the equality of variances for each and every variable calculated for the two groups. Data were analysed by Statistical Package for Social Sciences version 18.0 statistical analysis software and graphs were made using GraphPad Prism 7 software. A value of $P < 0.05$ is considered significant.

Results

A total of 50 cases were enrolled, of which 48 patients completed the study. Two cases were excluded which included one patient in Group IT due to inadequate level of spinal blockade, and one patient in Group NB due to failure of FSNB, necessitating administration of general anaesthesia. Both groups were comparable regarding age, sex,

weight, ASA status or duration of surgery although, more number of males were studied in each group [Table 1].

Table 1: Demographic data

Patient characteristic	Group IT	Group NB	*P*
Age (years)	29.38(±6.22)	26.50(± 5.66)	0.10
Sex (male/female)	22/2	23/1	0.56
Weight (kg)	67.33(± 4.58)	66.42(±4.82)	0.50
ASA status (1/2)	20/4	22/2	0.39
Duration of surgery (min)	105.17(±13.00)	107.63(±12.64)	0.51

ASA = American Society of Anaesthesiologists

Onset of sensory and motor block was significantly earlier in Group IT in comparison to Group NB (P<0.001) [Table 2]. Haemodynamic parameters showed statistically significant differences (P<0.05) between 45-90 min intraoperatively, with Group IT showing decreased pulse rate and mean arterial pressure from baseline values in comparison to Group NB [Figure 1]. No statistically significant differences in haemodynamic and respiratory parameters were found between the groups in postoperative period.

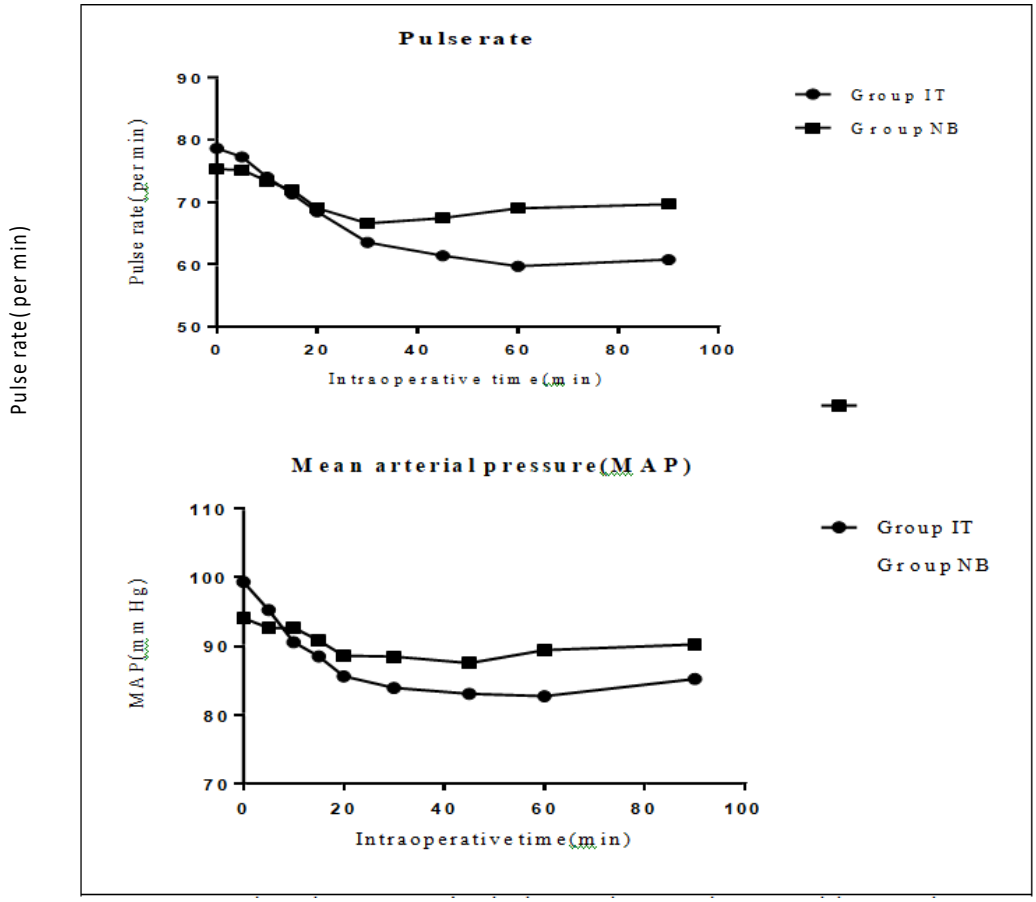

Figure 1: Haemodynamic parameters showing lesser pulse rate and mean arterial pressure in Group IT in comparison to Group NB, especially during the latter half of intraoperative period

Table 2: Block characteristics

Characteristic of block	Group IT	Group NB	*P*
Onset of block			
Temperature (min)	5.63(±0.77)	6.58(±0.83)	< 0.001
Pin prick (min)	9.08(±1.18)	12.75(±2.15)	< 0.001
Motor (min)	12.50(±1.35)	19.04(±2.25)	< 0.001
Duration of block			
Motor blockade (min)	180.33(±13.20)	264.88(±14.87)	< 0.001
Sensory blockade (min)	288.29(±15.86)	469.58(±15.17)	< 0.001

Duration of sensory and motor blockade in Group NB was significantly higher (P<0.001) than Group

IT [Table 2]. The mean postoperative pain-free period was much higher in Group NB (P<0.001) than in Group IT [Table 3]. The rescue analgesic requirement was significantly less (P<0.05) in Group NB as shown by total 24h rescue analgesic [Table 3] and mean 24h rescue analgesic frequency [Figure 2].

None of the patients in either group required a second rescue analgesic. An increase in mean sedation scores were noted in both the groups after 15 min of drug administration, in the first 6h postoperatively, but was not associated with airway compromise or desaturation. Mean sedation scores in the first 6 h postoperatively was found to be higher in Group IT in comparison to Group NB (P<0.05) [Table 3].

Table 3: Postoperative analgesia and sedation

	Group IT	Group NB	*P*
Pain-free period (min)	325.33(±17.85)	522.08(±21.18)	< 0.001
24 h rescue analgesic (mg)	100.0(±36.12)	71.88(±26.89)	0.004
Sedation score (6 h)	2.58(±0.50)	2.29(±0.46)	0.043

Figure 2: Mean rescue analgesic frequency in the postoperative period (24 h) showing less analgesic requirements in Group NB in comparison to Group IT

Discussion

Clonidine, when added to bupivacaine in FSNB, showed longer pain-free period and lesser total rescue analgesic consumption than when it is added to bupivacaine intrathecally. Clonidine was used in a dose of 1 μg/kg as this dose has been safely used.[8,9]

Current advances of pain therapy have focused on either improving drug formulations or catheter systems for local infiltrations or improve performance of regional anaesthetic techniques. These advances have the potential for side effects from catheter migration after home discharge.[10] An ideal adjuvant, permitting single administration, and not causing systemic side effects, prolonging sensory blockade without increasing motor blockade duration is needed for adequate pain relief. Effect of clonidine along with bupivacaine was compared through two different routes-intrathecal and FSNB, and the route with better perioperative outcome was sought. Patients of Group IT had a much earlier onset of sensory and motor block than in patients of Group NB. Haemodynamic parameters were maintained closer to baseline values in case of Group NB; whereas Group IT showed lesser pulse rate and mean arterial pressure, especially during the latter half of intraoperative period. Addition of clonidine to bupivacaine in nerve block resulted in satisfactory prolongation of analgesic duration of 522.08(±21.18) min giving a pain-free duration of about 9 h. Intrathecal clonidine with bupivacaine improves the duration of motor block and analgesic quality without delay in ability to void or readiness for home discharge following knee arthroscopy[11] but central neuraxial techniques themselves prolong home discharge when compared to wound infiltrations or general anaesthesia alone.[10] Strebel et al.[8] compared 37.5, 75 and 150 μg of intrathecal clonidine and found that intrathecal clonidine produced dose dependent increase in spinal anaesthesia and pain relief without any untoward side effect. Cucchiaro and Ganesh[4] reported mean motor block of 9.6 h after addition of clonidine 1 μg/kg to local anaesthetic in peripheral nerve block but the assessment of block characteristics might differ from our study due to

the retrospective nature of the study and interference from variety of peripheral nerve blocks included. Prolonged motor block may adversely affect hospital discharge as it delays neurological examination. We report an increase in motor blockade duration lesser than those reported by Cucchiaro and Ganesh[4] and hence no significant increases in hospital stay were observed probably due to low concentration of clonidine used (0.5 μg/kg in each block). FR Montes et al.[7] concluded that combined sciatic-femoral nerve block for outpatient arthroscopic knee surgery offered satisfactory anaesthesia, with a clinical profile similar to that of low-dose spinal anaesthesia. Sciatic-femoral nerve blocks were associated with significantly lower pain scores during the first 6 postoperative hours. We report a better clinical profile in Group NB patients in terms of stability of haemodynamic and respiratory parameters, increased duration of sensory block and pain-free interval, lesser 24 h rescue analgesic requirements and low sedation scores. Neeru Sahni et al.[2] concluded that clonidine in a dose of 1 μg/kg was safe and effective adjuvant with bupivacaine in prolonging analgesia through various routes (intrathecal, femoral-sciatic nerve block, intra-articular) employed for post knee surgery pain. The maximum prolongation of analgesia was found to be achieved through FSNB route.

Clonidine potentiates the sensory and motor block of intrathecal local anaesthetics by 30-50% and is more effective for dynamic pain control while opioids are effective for pain at rest.[12,13] Hence, clonidine might be effective for permitting early movement especially in the ambulatory setting. Clonidine inhibits the release of substance P in the spinal cord, activates inhibitory G-proteins at spinal and supraspinal sites within the central nervous system and suppresses neurotransmission in peripheral sensory Aδ and C nerve fibres. In nerve blocks, clonidine may also produce local vasoconstriction, resulting in a delayed absorption of local anaesthetic and block prolongation apart from directly binding to α2-adrenergic receptors located on primary afferent terminals, on neurons in the superficial laminae of the spinal cord and several brainstem nuclei implicated in analgesia.[4,14]

Haemodynamic and sedation effects of clonidine are more common in higher doses.[14] Though mean sedation scores in the first 6 postoperative h was found to be higher in Group IT in comparison to Group NB, it was not clinically significant, similar to the study on intrathecal clonidine in doses of 37.5, 75, and 150 μg/kg.[8] Bupivacaine alone in nerve block shows lower pain scores in the initial 6 h of postoperatively, but a comparable postoperative analgesia with the intrathecal route later.[7] Hence, addition of clonidine in nerve block significantly improved postoperative analgesia and decreased rescue analgesic requirement in comparison to intrathecal route.

A significant finding of our study is that we are using 0.25% bupivacaine with 1μg/kg clonidine in FSNB route and able to produce motor blockade (Stage 2 of Modified Bromage Scale) required for the surgery to proceed. Thus we are using half the concentration of local anaesthetic required otherwise to produce motor blockade, thereby minimising the potential chances of any local anaesthetic toxicity, besides being economical.

The limitation of using 0.25% bupivacaine is delay in onset of motor block (19.04 ±2.25 min) which in turn delays starting of the operation. Another limitation of our study is that it is not blinded, so neither the participant's nor the observer's bias could be eliminated from the study.

Conclusion

Clonidine in a dose of 1 μg/kg with bupivacaine has more favourable perioperative outcome in femoral-sciatic nerve block route in comparison to its use via intrathecal route in arthroscopic knee surgery. It provided stable haemodynamic and respiratory parameters intra and postoperatively, increased duration of sensory block and pain-free period, lesser 24 h rescue analgesic requirement making it ideal for post knee surgery pain.

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