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THE EFFECTS OF INTRAVENOUS PARACETAMOL ON THE QUALITY OF POSTOPERATIVE ANALGESIA IN PATIENTS UNDERGOING INGUINAL HERNIA REPAIR UNDER SUBARACHNOID BLOCK: A PROSPECTIVE RANDOMIZED CONTROL TRIAL

Anaesthesiology

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ABSTRACT

Spinal anaesthesia is safe and effective method of anaesthetic practice for infra umbilical surgeries. Commonly used drugs to alleviate postoperative pain after surgery include opioid, nonsteroidal anti-inflammatory drugs (NSAIDS), and paracetamol. The purpose of this prospective randomized double-blind clinical study is to assess the effect of intravenous paracetamol on duration of post operative analgesia, when administered intra operatively after subarachnoid block, using hyperbaric bupivacaine. After obtaining approval of the institutional ethical committee and written informed consent from the patients, a prospective randomized double blind study was undertaken with 98 ASA I-II patients, aged between 18 to 60 years, scheduled for elective inguinal hernia surgeries under spinal anaesthesia. In our study the time to first request for postoperative analgesic was significantly prolonged in group P (163.98 ± 16.86 mins) as compared to group C (134.59 ± 16.45mins) ($p<0.001$). Total number of rescue analgesic doses in 24 hours was significantly lower in group P (2.47±0.54) compared to group C (3.39±0.97) ($p<0.001$). Mean VAS score in first 24 hours was significantly lower in group P (1.42±0.145) compared to group C (1.82± 0.11) ($p<0.001$). We concluded that 1 gm intravenous paracetamol is safe and effective method of providing postoperative analgesia for first 24 hours, in patients undergoing infra umbilical surgeries under spinal anaesthesia.

KEYWORDS

Spinal anaesthesia, Paracetamol, Bupivacaine

INTRODUCTION

Spinal anaesthesia is safe and effective method of anaesthetic practice for infra umbilical surgeries. Bupivacaine is drug of choice for spinal anaesthesia for procedures lasting upto 2 to 2.5 hours. Post operative pain is most frequent complain of patients due to surgical trauma. Various adjuvaants were used with local anaesthetic to increase pain free period post operatively. These adjuvants may hasten onset as well as prolonged duration of sensory and motor block, which results into prolong postoperative analgesia.

Commonly used drugs to alleviate postoperative pain after surgery include opioid, nonsteroidal anti-inflammatory drugs (NSAIDS), and paracetamol. In most post anaesthesia care units (PACU), opioids are considered as the primary modality of analgesic therapy to alleviate moderate to severe postoperative pain. However, opioids does not provide optimum patient satisfaction as they are associated with dose-related adverse effects such as sedation, respiratory depression, cardiovascular depression, postoperative nausea, vomiting, pruritus, and urinary retention.[1,2] NSAIDS may be alternate option in PACU to reduce postoperative pain without cardiovascular or respiratory depression. Although NSAIDS have been associated with adverse effects such as peptic ulceration, gastritis, and renal impairment.[3,4,5] Paracetamol is devoid of such gastric problems as it does not alters the gastric mucosal barrier, thus it might be analgesic of choice where other NSAIDS contraindicated.[4,5,6]

The purpose of this prospective randomized double-blind clinical study is to assess the effect of intravenous paracetamol on duration of post operative analgesia, when administered intra operatively after subarachnoid block, using hyperbaric bupivacaine. This study was based on assumption that intraoperative intravenous paracetomol, may prolong the duration of postoperative analgesia and reduce postoperative analgesic requirement after spinal anaesthesia.

MATERIAL AND METHODS

After obtaining approval of the institutional ethical committee and written informed consent from the patients, a prospective randomized double-blind study was undertaken with 98 ASA I-II patients, aged between 18 to 60 years, scheduled for elective inguinal hernia surgeries under spinal anaesthesia. Patients with known contraindication to spinal anaesthesia, the study drug, patients using α_2-adrenergic receptors antagonists, calcium channel blockers, angiotensin converting enzyme inhibitors, body weight more than 120Kg, history of hepatic, renal, cardiopulmonary disease, hypertension, diabetes, and asthma were excluded.

A day prior to surgery, pre-anaesthetic evaluation was done with special consideration to elicit a history of hypertension, dyspnoea, chest pain, cough, wheezing, convulsions, diabetes mellitus as well as previous anaesthetic history and drug sensitivity. Patients were advised for nil by mouth for 6 hours prior to surgery. Tablet alprazolam 0.25 mg and tablet ranitidine 150 mg was given orally on the previous night and in the morning on the day of surgery. Intravenous access was secured and infusion of Ringer's lactate solution was started. Patients were then shifted to the operating room after which routine non-invasive monitors were applied and vital were recorded. After preloading the patients with Ringers Lactate 15 ml/kg, lumbar puncture was performed at L3-4 level with Quincke type 25gauge spinal needle via midline approach with patients in the sitting position, under full aseptic precaution. Bupivacaine hyperbaric 3 ml solution was injected intrathecally after confirming free flow of CSF. Patient was kept in supine position to achieve bilateral block.

The study participants were randomly divided into two groups by a computer generated random number. Group P (n=49) receiving 1g/100ml intravenous paracetamol infusion over 15 min after subarachnoid block and group C (n=49) receiving intravenous normal saline 100 ml over 15 minutes, after subarachnoid block. Anaesthesiologist A was responsible to prepare study drugs, Anaesthesiologist B was responsible to monitor the heart rate, non invasive blood pressure, sensory level, pain (Visual analogue scale), motor block (modified Bromage scale) intraoperatively and upto 24 hours after spinal anaesthesia. Anaesthesiologist C was responsible for study drugs administration (intravenous and intrathecal) to the patients. Anaesthesiologist A and C were kept constant throughout the study. Anaesthesiologist B, C and the patient were kept unaware of the

drug injected to enable double-blinding.

Level of sensory loss was assessed by pin-prick test in every 2 minutes till it reaches the highest level and then every 15 minutes during surgery and postoperatively. Motor blockade was assessed every 2 min before the surgery starts and then postoperatively every 30 min till the modified bromage scale score returns to zero. Systolic blood pressure, diastolic blood pressure, heart rate and oxygen saturation (SpO2) were monitored regularly and for study purpose before, after subarachnoid block, in every 15 minutes intraoperatively then and for 30min, 6 hour, 12 hour and 24 hour postoperatively. Surgery was initiated when the level of sensory block reached to T_{10} dermatome level or above and attainment of complete motor block. Otherwise it was considered as failed spinal and alternate technique of anaesthesia was chosen and case was excluded from study. Heart rate below 60 beats per minute was considered as bradycardia and treated with incremental doses of injection atropine 0.4 mg intravenous. Any fall in the systolic blood pressure below 90mm Hg or fall greater than 20% of baseline was treated with mephentermine 6 mg intravenous.

Postoperative pain was assessed by using the visual analogue scale (VAS). VAS was assessed every 30 minutes for 6 hours, then every 2 hours up to 12 hours and 4 hourly up to 24 hours. Injection tramadol 2 mg per kg intravenously was given as rescue analgesic. Time for first rescue analgesic was noted and total 24 hours analgesic requirement was calculated. All durations were calculated using time of spinal injection time as zero.

To calculate the sample size, with 90% power and 5% probability of type 1 error, it was estimated that 49 subjects per study group were required, assumed standard deviation of 90 minutes for this study. The Statistical software Epi Info 6 was used for the analysis of the data and Microsoft word and Excel was used to generate graphs, tables etc. Age, height, duration of surgery, onset and duration of sensory and motor block, VAS score, time of demand of rescue analgesic, total consumption of rescue analgesic were compared using student paired 't' Test.

RESULTS

There were no significant differences between the groups, with respect to demographic characteristics like age, weight, ASA grade and duration of surgery (Table 1).

Table No. 1- Demographic Characteristics

	Group P (n=49)	Group C (n=49)	P value
Age (years)	44.37±12.66	41.98±13.86	0.376
Weight (kg)	57.32±4.92	58.71±3.04	0.09
ASA physical status (I: II)	34:15	37:12	0.828
Duration Of surgery (min)	77.95±7.494	80.61±8.93	0.114

In present study highest level of sensory block was higher in paracetamol group (6.98±0.69 thoracic dermatome) compared to control group (7.63±0.60 thoracic level) and was statistically significant ($p<0.001$). Mean duration of two dermatomal regression of sensory block (135.92±10.69 v/s 88.78 ± 7.67 mins) and duration of sensory blockade i.e. time for regression to S1 dermatome (197.35 ± 9.25 v/s 152.76 ± 8.6 min) were significantly prolonged in paracetamol group as compared to control group ($p<0.001$) [Table 2, Figure 1].

Table-2: Comparison of sensory-motor blockade and analgesia in both groups

	Group P (n=49)	Group C (n=49)	P value
Peak sensory Level (T-Thoracic)	T 6.98±0.69	T 7.63±0.60	< 0.0001
Time to achieve Peak sensory Level (min)	9.34±0.77	9.59±0.67	0.08
2 segment regression of sensory blockade (min)	135.92±10.69	88.78±7.67	< 0.0001
Duration of sensory blockade (min)	197.35±9.25	152.76±8.60	< 0.0001
Onset of motor blockade (min)	5.02±0.72	5.33±0.90	0.066
Duration for motor block (min)	156.53±11.79	128.78±12.01	< 0.0001
VAS	1.42±0.145	1.82±0.11	< 0.0001
Time of rescue analgesia (min)	163.98±16.86	134.59±16.45	< 0.0001
Total no. of rescue dose in 24 hr	2.47±0.54	3.39±0.97	< 0.0001

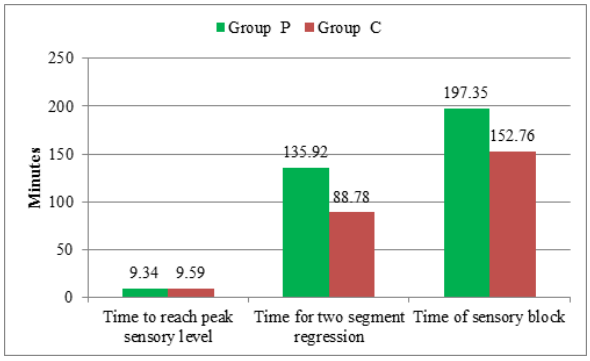

Figure-1: Comparison of time to reach peak sensory level, time for two segment regression, duration of sensory block

In our study the time to first request for postoperative analgesic was significantly prolonged in group P (163.98 ± 16.86 mins) as compared to group C (134.59 ± 16.45mins) ($p<0.001$). Total number of rescue analgesic doses in 24 hr was significantly lower in group P (2.47±0.54) compared to group C (3.39±0.97) ($p<0.001$). Mean VAS score in first 24 hours was significantly lower in group P (1.42±0.145) compared to group C (1.82± 0.11) ($p<0.001$) [Table 2, Figure 2]. Onset of motor block was comparable among the groups (p 0.001) and duration of motor block was significantly higher in paracetamol group ($p<0.001$) [Table 2].

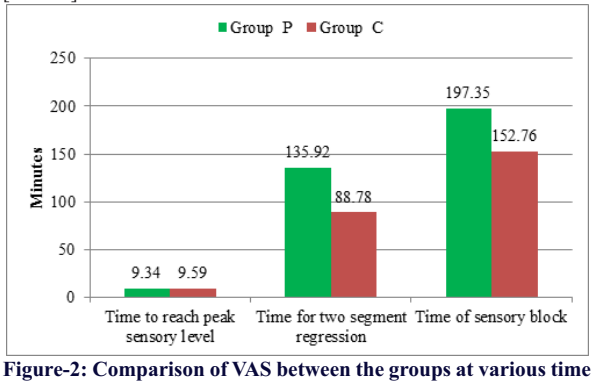

Figure-2: Comparison of VAS between the groups at various time intervals

DISCUSSION

Our study demonstrates that 1gm iv paracetamol infusion after spinal anaesthesia with bupivacaine reduce postoperative VAS score, number of demand and dose of rescue analgesic and prolong sensory block and two dermatomal regression after elective inguinal hernia repair surgery.

Previous studies shows that when iv paracetamol used during perioperative period, improve quality of anaesthesia and reduce postoperative analgesic requirement.[7,8,9] Study done by Bhattacharya et al[7] demonstrate that intravenous paracetamol infusion increase duration of sensory block and time to first analgesic requirement in major gynaecological surgeries under spinal anaesthesia. Khalili G et al[8] compared the efficacy of preemptive and preventive iv paracetamol and found that postoperative analgesic consumption was reduced in preemptive paracetamol group. Hynes et al[9] also found that total pain relief score (TOTPAR) was significantly high in paracetamol group in patients undergoing hip arthroplasty under spinal anaesthesia. Another study done by Sinatra et al[10] they found that morphine consumption over 24 hours was significantly reduced in study group.

Although mechanism of prolongation of sensory block remain unclear, the main mechanism of analgesic effect of paracetamol, through its action on central nervous system mediated by inhibition of prostaglandin synthesis and selective inhibition of cyclooxygenase 2(COX 2) enzyme.[11,12,13,14] Another probable mechanism, that

paracetamol modulates the endogenous cannabinoid system in brain and spinal cord. Paracetamol metabolized in to N-arachidonylphenolamine (AM404)[15,16] which inhibits uptake of the endogenous cannabinoid/vanilloid anandamide by neurons. Anandamide play major role in perception of pain.[16,17,18,19] Also AM404 inhibits sodium channels, as do the anesthetics lidocaine and procaine.[7,15] Some author also demonstrate alternate mechanism of action, by inhibition of nitric oxide (NO) production. NO generated by activation of L-arginine/NO pathway by substance P and it is important neurotransmitter of nociception at the level of spinal cord.[20,21] Above mention mechanisms might be possible mechanism of action of paracetamol to reduce post oprerative pain.

In our study, we monitor heart rate and blood pressure throughout during study period, shows that paracetamol does not have any cardiovascular effects. However, in paracetamol group heart rate and blood pressure remain lower during intraoperative period, but remain comparable among the groups. Over all incidences of adverse effects did not show any statically significant difference between two groups. In paracetamol group (3/49) had intraoperative heart rate <60/min as compared to control group (2/49). However, bradycardia was transient in most of these patients responded well to atropine. In paracetamol group (6/49) patients had systolic BP <90 mm Hg, as compared to control group (4/49), which was successfully managed by iv fluids and mephentermine. The incidence of hypotension as well as total dose requirement of mephentermine for management of hypotension was quite comparable among the groups. In our study there were no incidence of nausea and vomiting during study period.

CONCLUSION

We concluded that 1 gm intravenous paracetamol is safe and effective method of providing postoperative analgesia for first 24 hours, in patients undergoing infra umbilical surgeries under spinal anaesthesia.

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