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CLINICAL EFFICACY OF TRAMADOL AS AN ADJUVANT TO CHLOROPROCAINE IN SPINAL ANAESTHESIA FOR INFRA-UMBILICAL SURGERIES: A PROSPECTIVE RANDOMIZED DOUBLE BLIND STUDY

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ABSTRACT

Introduction: Spinal anaesthesia is a reliable and safe technique for procedure of the lower abdomen and lower extremities. Aim of this study to evaluate the effect of tramadol as an adjuvant with intrathecal isobaric chloroprocaine in infraumbilical surgeries. **Material &Methods:** Clinical Trials Registry India (CTRI/ 2019/04/018539) registration and taking informed written consent from the patients, this prospective, double blind study in patients with ASA grade I and II of either sex, age 18-60 years, posted for Infra-umbilical surgeries under spinal anaesthesia was carried out at our institute. Eighty patients were randomly divided into two groups (n=40): Group (CT)- Patients received 1% Chloroprocaine 4 ml (40 mg) + Tramadol 0.5 ml (25 mg) total volume 4.5 ml. Group (CS)- Patients received 1% Chloroprocaine 4 ml (40 mg) + Normal Saline 0.5 ml total volume 4.5 ml. Sensory and motor block characteristics, vital parameters and any adverse effects were noted in a performa. **Results:** Time to sensory block regression to S_1 was significantly longer in group CT (123.98±9.34min) as compared to group CS (108.85±8.56min). Time to first rescue analgesia was significantly longer in group CT (92.45 ±9.64 min) as compared to group CS (84.75±8.43min). Time to motor block regression to B_0 was significantly longer in group CT (105.80±7.91min) as compared to group CS (87.60±8.07min) [P=0.000]. Both the groups were statistically comparable regarding vital parameters during intra-operative period [P>0.05]. **Conclusion:** Hence we recommend the addition of Tramadol (25 mg) as an adjuvant to isobaric Chloroprocaine 1% (4ml) for the patients undergoing infraumbilical surgeries under subarachnoid block.

KEYWORDS: Chloroprocaine, Tramadol, Infraumbilical surgery, Subarachnoid block.

INTRODUCTION

Spinal anaesthesia is a reliable and safe technique for procedure of the lower abdomen and lower extremities. Nevertheless, some of its characteristics may limit its use for ambulatory surgery, including delayed ambulation, risk of urinary retention, and pain after block regression.[1] The short duration of the procedure and high turnover in a day-care center necessitate the performance of neuraxial anaesthesia with local anaesthetic that exhibit fast onset and quick recovery kinetics.[2] Various adjuvants have been used to increase the potency of local anaesthetics without any side effects like ketamine, midazolam, opioids, alfa-2 agonists etc. Tramadol a centrally acting opioid has been used as an additive to epidural and intrathecal local anaesthetics as it is not associated with as much respiratory depression as other opioids.[3,4] Addition of tramadol to intrathecal bupivacaine significantly prolonged the duration of analgesia.[5] As Chloroprocaine is ultra-short acting local anaesthetic and till date there are limited studies of Chloroprocaine with adjuvants so we planned this study to evaluate the effect of tramadol as an adjuvant with intrathecal isobaric chloroprocaine in infra umbilical surgeries.

MATERIAL AND METHODS

After taking institutional ethical committee clearance and Clinical Trials Registry India (CTRI/ 2019/04/018539) registration and taking informed written consent from the patients for participation, this prospective, randomized, double blind case-control study was carried out in the Department of Anaesthesiology of our institute.

Sample size: The sample size was calculated on the basis of previous study by Vath JS et al[6] (2004) where duration of complete regression of sensory block was 104 ± 7 min in Fentanyl group and 95 ± 9 min in control group. A minimum sample size of 21 subjects in each group was required to study a difference of 9 min in analgesia at Confidence Limit of 95% and power of 95 %. Rounding off a sample size of 30 in each group was required which also fulfill the criteria of central limit theorem. We have taken 40 patients in each group to compensate drop-outs.

Inclusion Criteria: Patients with ASA physical status Grade I and II of either sex, Patients in the age group of 18-60 years, Posted for Infra-umbilical surgeries under spinal anaesthesia. Exclusion criteria: Patients posted for emergency surgeries, Pregnant patients, Patients having coagulation abnormalities, platelet count <75,000, INR >1.5, or on anticoagulants, Patients having systemic illness (like severe hypovolemia, raised intracranial pressure, neuromuscular diseases, ischemic/ valvular/ congenital heart diseases, psychiatric, hematological disorder), Patients having any absolute contraindications for spinal anaesthesia, Patient refusal to participate in study, Any allergy to local anaesthetic or Tramadol, Short stature (height <150cms), with spinal deformity.

Group allocation: All patients under study were subjected to a detailed pre-anaesthetic examination and investigations were carried out during this evaluation. Patients who fulfill inclusion criteria were enrolled in the study. They were randomly divided into two groups of 40 patients in each group using sealed envelope technique- Group I (CT)- Patients received 1% Chloroprocaine 4 ml (40 mg) + Tramadol 0.5 ml (25 mg) total volume 4.5 ml. Group II (CS)-Patients received 1% Chloroprocaine 4 ml (40 mg) + Normal Saline 0.5 ml total volume 4.5 ml.

Blindness: Two anaesthesiologists were involved in the study. Drugs prepared by one anaesthesiologist as per group allocation who was not further involved in the study. The anaesthesiologist who conducted the study himself performed all subarachnoid blocks and recorded all data, was not aware about which drug regime had been administered to the patient. Patient, surgeon, and postoperative ward nurse were also not aware of group allocation.

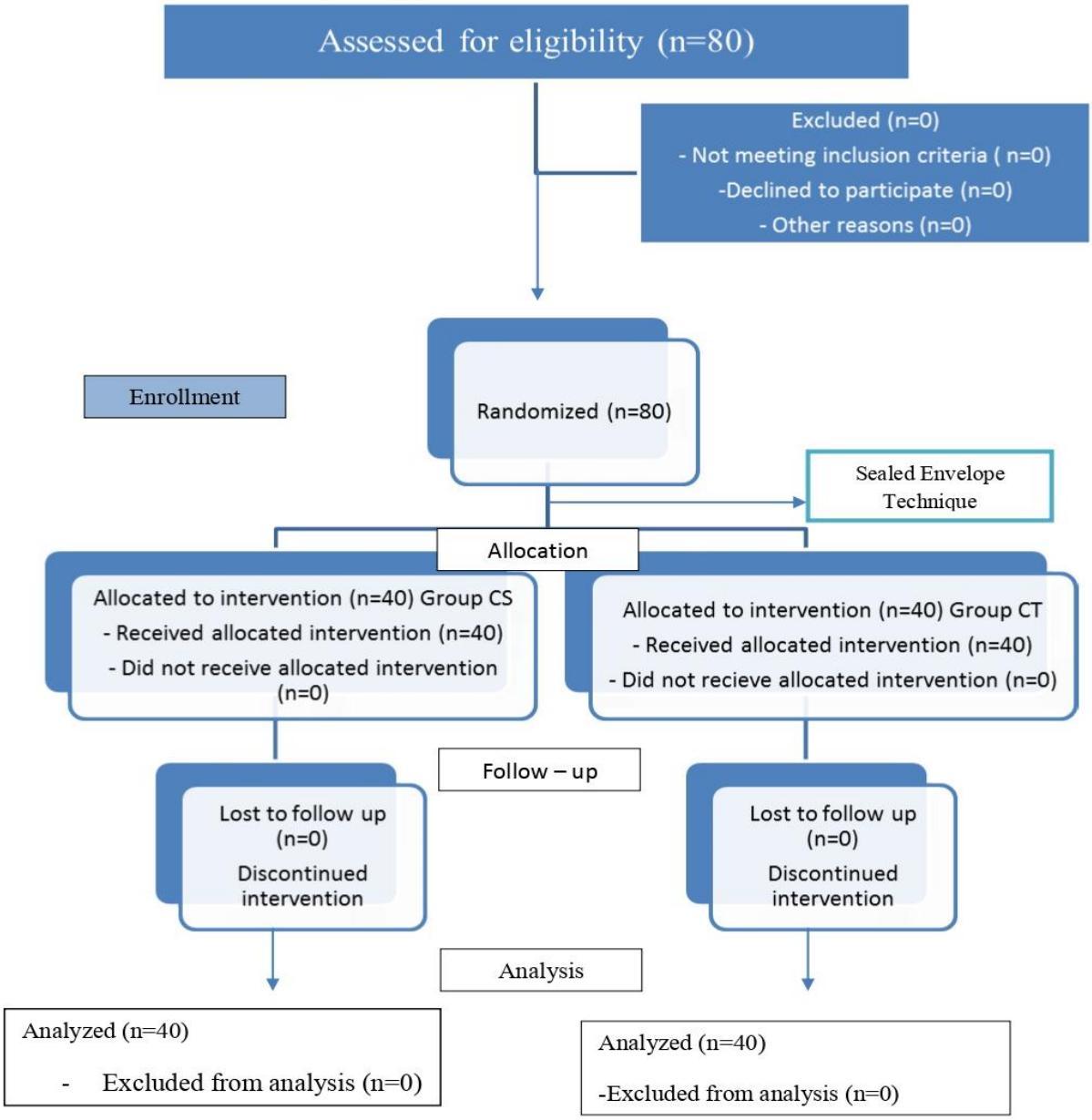

Fig. Consort Flow Chart.

Spinal anaesthesia technique: Elective patients were kept overnight fasting. One night before surgery tab. Alprazolam 0.25 mg, tab. Ranitidine 150 mg given. In the morning chlorhexidine mouth wash was done and then 2 hours before the surgery capsule omeprazole 20 mg given with sip of water. On arrival to operation room standard monitoring pulse oximeter (SpO_2), noninvasive blood pressure (NIBP), and electrocardiogram (ECG) were applied and patient's baseline vitals heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and peripheral oxygen saturation (SpO_2) were recorded. After securing 20G peripheral I.V. cannula, preloading with 500 ml Ringer lactate was done in all cases. Using strict aseptic technique, Sub-arachnoid Block was performed at L_3-L_4 interspace with patient with lateral position using a 25-gauge Quincke's spinal needle via midline approach and keeping bevel up. After getting free flow of cerebrospinal fluid, Intrathecal drug administered as per group allocation and sterile dressing was applied. End of spinal injection was taken as time zero for all further data recording. Oxygen at a rate of 5 L/min was administered via a face mask. All data were recorded in a proforma. Sensory block was assessed by pin prick method using a short beveled 24G needle checked bilaterally in mid-clavicular line and no perception to pin prick was considered as sensory block. Motor block was assessed using Modified Bromage scale (0 = no motor block, able to flex hips/ knees, ankles; 1 = able to move knees and ankle, unable flex hip i.e. unable to raise extended legs (partial motor block); 2 = able to flex ankles, unable to flex hip/knee (almost complete motor block); 3 = unable to move any part of the lower limb (complete motor block). Sensory and motor block was assessed every 2 min after intrathecal injection till T_{10} level and maximum Bromage score of 2 or 3 is achieved, which is criteria to allow start of surgery. If pain at surgical site at 15 min and Bromage score is 0 or 1 then the case was declared as failed spinal and proceeded with conversion to general anaesthesia, and excluded from the study. Time to reach T_{10}, (sensory onset), peak sensory level, time to peak sensory level, maximum Bromage score, time to maximum Bromage score (motor onset) recorded. Vital parameters blood pressure (SBP, DBP, and MAP), HR and SpO2 were recorded at every 2 min till 10 min then every 5 min till completion of surgery.

Hypotension and vasopressor requirement: Hypotension defined as fall in MAP of >20% from baseline value and treated with Inj. Mephentermine 6 mg in graded dose till desired effects achieved. Bradycardia defined as fall in HR < 60/min and treated with Inj. Atropine 0.3 mg in graded dose till desired effects achieved. Requirement of vasopressor (number of doses and amount) were recorded in each case. If patient or surgeons have complaints about inadequacy of anaesthesia, supplementation was given as Fentanyl/ Midazolam. Sensory level and Bromage score were recorded at the end of surgery and assessed at every 30 minutes till sensory regression to S_1 (return of sensation at lateral side of foot), Bromage score return to zero, and was defined as duration of sensory and motor block respectively. Time of first pain was defined as duration of analgesia and Inj. Diclofenac 75 mg IM was given as per institutional protocol. Vitals parameters (SBP, DBP, MAP, and HR) were recorded at 30 min interval in postoperative period. Any occurrence of complications in postoperative period were noted and treated accordingly.

Statistical Analysis: Data were entered in MS EXCEL and analyzed using SPSS version 20. Categorical data were presented as number (proportion), and compared with chi-square test. Continuous variables were presented as Mean ± SD and compared using t-test as per need. $P < 0.05$ were considered statistically significant.

RESULTS

Table 1: Demographic parameters.

Variables	Group CT(n=40)	Group CS(n=40)	P value
Age(years)	52.75±11.25	49.75±12.85	0.482
Sex Male Female	34(85%) 06(15%)	35(87.5%) 05(12.5%)	0.75
Height(cm)	160.10±06.15	162.45±06.45	0.099
Weight (kg)	62.02±8.71	65.55±10.37	0.104

Data are expressed as mean ± SD

Both groups were statistically comparable regarding mean age, mean sex, mean height, mean weight.[p>0.05]

Table 2: Sensory block characteristics.

	Group CT (n=40)	Group CS (n=40)	P value
Time to reach T10 sensory level (min)	5.95±1.66	6.32±1.64	0.313
Peak Sensory Level	7.10±1.94	7.58±1.23	0.93
Time to reach PSL (min)	10.45±2.77	10.68±2.79	0.718
Duration of Sensory Block i.e. Time to regress to S1(min)	123.98±9.34	108.85±8.56	0.000
Duration of Analgesia i.e. Time for first rescue analgesia (min)	92.45±9.64	84.75±8.43	0.000

Data expressed as mean ± SD

Table 2 shows that time to sensory block regression to S_1 was significantly longer in group CT (123.98±9.34min) as compared to group CS (108.85±8.56min) [p=0.000]. Time to first rescue analgesia was significantly longer in group CT (92.45 ±9.64 min) as compared to group CS (84.75±8.43min) [p=0.000]. This implicates that addition of tramadol to chloroprocaine results in significant prolongation of duration of sensory block & duration of analgesia.

Table 3: Motor block characteristics.

	Group CT	Group CS	P value
Time to B_3 (Bromage score 3)	6.90±1.57	9.10±1.75	0.000
Duration of motor block Time to regression to B_0 (Bromage score 0) Mean ± SD	105.80±7.91	87.60±8.07	0.000

Table 3 Shows that mean time to reach B_3 was significantly shorter in group CT (6.90 ±1.57 min) as compared to group CS (9.10±1.75 min) [p=0.000]. Time to motor block regression to B_0 was significantly longer in group CT (105.80±7.91min) as compared to group CS (87.60±8.07min) [p=0.000]. This implicates that addition of Chloroprocaine to Tramadol results in significant faster onset of motor block & prolongation of duration of motor block.

Table 4: Intraoperative side effects.

	Group CT(n=40)	Group CS(n=40)	P value
Hypotension	3	3	0.538
Bradycardia	1	0	0.314
Nausea/Vomiting	2	1	0.556

Test used –‘ chi square’ test

Table 4 shows that during the study period adverse effects were observed: 3 patients had hypotension and no patients had bradycardia and 1 patient had vomiting in group CS. While in group CT 3 patients had hypotension, 1 patient had bradycardia and 2 patients had nausea/ vomiting. These were successfully treated with single dose of mephentermine 6 mg, inj. Atropine (0.4 mg) and inj. Ondansetron 4 mg respectively. Incidence of hypotension, bradycardia, and vomiting were minimal and statistically comparable in two groups [p> 0.05].

Hemodynamic parameters: In our study, HR, SBP, DBP, and SpO_2 showed no significant change from baseline during intraoperative period between both the groups. Both the groups were statistically comparable regarding vital parameters like heart rate, systolic blood pressure, diastolic blood pressure mean arterial blood pressure and SpO2 during intra-operative period (p>0.05). This showed that chloroprocaine with tramadol in spinal anaesthesia produces effective sensory motor blockade without affecting hemodynamic variables significantly.

DISCUSSION

In this study, we have evaluated the efficacy of tramadol as an adjuvant to intrathecal isobaric chloroprocaine for elective infraumbilical surgeries. Vath JS et al., Casati A et al., Zahid F et al.[6-8] concluded that Chloroprocaine in spinal anaesthesia provides rapid onset and adequate potency, so preferred in ambulatory surgery.

Sensory Onset: In our study, when Tramadol was used with chloroprocaine in Group CT as an adjuvant mean time to reach T_{10} sensory level was 5.95 ± 1.66 min and mean time to reach peak sensory level was 10.45 ± 2.77 min, whereas when normal saline was used with chloroprocaine (Group CS) , mean time to reach T_{10} sensory level was 6.32± 1.64 min and mean time to reach peak sensory level was 10.68 ± 2.88 min and sensory onset in terms of both time to T_{10} and time to peak sensory level was not significant in both groups (p= 0.313 & 0.093 respectively). Our results were in coherence with study done by Casati et al[7] in lower limb surgeries in which time to T_{10} was 8 min with chloroprocaine-30, 7 min with chloroprocaine-40 and 6 min with chloroprocaine-50 which were statistically comparable (p= 0.74).

Sensory block duration: We measured time to onset of sensory block to time taken for sensory regression to S1 (sensory block duration) which was 123.98±9.34 min in Group CT and was 108.85±8.56 min in Group CS. The difference was statistically significant [p=0.000] in two groups. Sensory block duration was long with tramadol and short with chloroprocaine alone. Similar to our study, Bhaskara et al[11],Tuenkens et al[12], Salhotra et al[13], studies have also shown prolongation in sensory block duration. We have used tramadol as intrathecal adjuvant in our study. Tramadol exists as the racemic (1:1) mixture of the (+) and (−) enantiomer. It has dual

mechanism of action. Tramadol also cause spinal inhibition of pain by decreasing the reuptake of norepinephrine and serotonin. It was suggested by other studies that tramadol may have local anaesthetic effects on peripheral nerves.[14]

Motor block (Onset & Duration): Onset of motor block is defined as time to reach Bromage score 3. Mean Time to reach Bromage score 3 was 6.9±1.57 min in group CT and was 9.1 ± 1.75 min. in group CS, which was statistically significant (p=0.000) in two groups. Addition of tramadol to chloroprocaine in spinal anaesthesia accelerated the motor onset. In our study time to return to Bromage 0 (duration of motor block) was 84.60 ± 8.066 min in group CS, 105.80±7.91 min in group CT. Motor block duration was significantly longer in group CT as compared to group CS (p=0.00). The difference was statistically significant between the both groups. The studies done by Vaghadia et al[15] show that addition of fentanyl as an adjuvant intrathecally has no significant effect on duration of motor block (p>0.05) and their results were contrary to our study, they were used low dose(2ml) as compare to our study(4ml).

Duration of Analgesia: In present study time to first rescue analgesic (first complaint of pain) in postoperative period was considered as duration of analgesia, which was 84.75±8.43 min in group CS, 92.45±9.64 min in group CT. The duration of analgesia was significantly longer in group CT as compared to group CS [p=0.000]. Our study clearly indicated that addition of intrathecal tramadol to chloroprocaine significantly prolong the duration of analgesia. Zahid et al[8] also reported that mean duration of analgesia was 185.61±12.42 min in group BT and 120.93±15.54 min in group BS. Group BT shows significantly longer duration of analgesia as compared to group BS (p<0.001). Similar to our study, Parthasarathy et al[16] reported that duration of analgesia was significantly longer in Group LT (310±127.49 min) as compared to group LS (131±40.51 min) (p< 0.01).

Clinical efficacy: In present study infraumbilical surgeries were accomplished in spinal anaesthesia in two groups using chloroprocaine alone (group CS), and with tramadol (group CT) without need of any supplementation. Hence success rate was 100% in two groups, because in our study peak sensory level of around T_7 and Bromage score of 3 was achieved in all patients. Previous studies have also shown that bupivacaine and lidocaine in spinal anaesthesia alone and with tramadol produced effective sensory motor block of sufficient duration to accomplish various surgeries without need of supplemental analgesia.

CONCLUSION

The present study concludes that the addition of Tramadol(25mg) as an adjuvant to isobaric 1% Chloroprocaine (4ml) administered intrathecally to patients undergoing infraumbilical surgeries results in a prolongation of sensory block, motor block and duration of analgesia when compared to Chloroprocaine alone. The addition of Tramadol 25 mg does not result in any increase in adverse effects. So, we recommend the addition of 25 mg Tramadol as an adjuvant to 4 ml of isobaric 1% Chloroprocaine for the patients undergoing infraumbilical surgeries under subarachnoid block.

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