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RANDOMIZED DOUBLE BLIND COMPARISON OF INTRATHECAL 2-CHLOROPROCAINE WITH FENTANYL AND 2- CHLOROPROCAINE WITH SALINE IN LOWER LIMB SURGERIES.

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ABSTRACT

Background/Aim :- The aim of this study was to evaluate the onset,duration, level of sensory and motor block, post-operative analgesia and adverse effect of adding fentanyl with 2-choloroprociane intratically. 2-choloroprociane is very short acting local anesthetic which provide rapid onset and reliable blockade, giving it positive profile for ambulatory surgery. To improve its quality of anesthesia and analgesia use of adjuvant is recommended.

Design:- Randomized double blind prospective study.

Method:- 70 patients were randomly divided in two groups. Group CS received 4ml(40mg) of 1% 2-CP with 0.4 ml NS and group CF received 4ml of 1% 2-CP with 0.4 ml (20 ug) of fentanyl intrathecally. Both the group were evaluated for level,duration, onset of sensory and motor block along with postoperative analgesia,sedation score, hemodynamic parameters, side effects were noted .All data were analyized using unpaired t-tis $P< 0.05$ was considered significant.

Results: The duration of sensory and motor block was found to be prolonged in fentayl group as compare to saline group ,time to first request for analgesia in postoperative period was earlier in saline group as compared to fentanyl group. Nausea and vomiting were noted in our study but none of side effects were found to be significant in either group.

Conclusion:- We found that combination of intrathecally fentanyl along with 2-choloroprociane increase duration of sensory and motor block without significant side effects.

KEYWORDS : Fentanyl Chlroprocaine Intrathical Saline

INTRODUCTION

Spinal anesthesia is one of the most reliable and simple of all anesthetic techniques. It is a safe and effective alternative to general anesthesia when surgical site is located on the lower extremities, perineum (e.g. surgery on genitalia or anus) or lower body wall (e.g. inguinal herniorraphy). Although low dose of long acting local anesthetic such as bupivacaine, ropivacaine and levobupivacaine as usually administered intrathecally, they are associated with significant delays in hospital discharge and less reliability of block efficacy, onset and spread[1-4].chloroprocaine is an amino ester local anesthetic with very short half-life. It was developed to meet the need for short acting spinal anesthetic that is reliable and has a favorable safety profile to support the need for day care surgery [4]. Its safety and reliability for spinal anesthetic has been reported since 1952[12].

When compared to lidocaine, low dose bupivacaine and articaine, 1% 2-chloroprocaine showed a better anesthetic profile for ultra short procedures[6,7]). The newer trend in regional anesthesia for ambulatory surgery is to use lower dose of local anesthetic providing segmental block with an adjuvant. Various adjuvants have been used with local anesthetics and evaluated in quest for an ideal one, which can enhance the quality of analgesia and prolong the duration of spinal anesthesia with minimal side effects [2].

The use of neuroaxial opioid has gained popularity over past few years as they enhance the spread of spinal anesthesia. It has been reported that the addition of intrathecal opioid to spinal anesthetics prolong sensory blockade without prolonging motor blockade[1,8]. Lipophilic opioid fentanyl is increasingly being administered intrathecally as adjunct to local anesthetics. It is a μ receptor agonist and 75-100 times more potent than morphine. It prolongs sensory blockade when given intrathecally but is also associated with side effects like pruritis, nausea and respiratory depression when used in large dose [2,8]).So we designed the study to compare the efficacy of 2-Chloroprocaine with saline and with fentanyl to intrathecal 1% 2-Chloroprocaine in lower limb surgeries lasting <60 min with respect to onset, duration and recovery of sensory and motor block and time to first request for post operative analgesia.

MATERIALAND METHOD

After obtaining approval from the Ethical committee of the hospital, this prospective randomized double blind study was conducted in the Department of Anesthesiology and Intensive care unit in tertiary care hospital on 70 patients of either sex with ASA 1 and 2 physical status and aged between 18-60 years, scheduled for lower limb surgeries including foot surgeries, ankle procedure, knee arthroscopy, tibial nail removal etc, with duration of ≤60 min.The patients were randomly divided into 2 groups. Group CF comprising 35 patients were received 4 ml of 1% 2-chloroprocaine(40 mg)and fentanyl (20μg) 0.4ml.Group CS comprising 35 patients were received 4ml of 1% 2-chloroprocaine (40 mg) and normal saline 0.4ml making total volume of 4.4ml.Exclusion criteria were Patients refusal for participating, Patients with contra indication to spinal anesthesia,Pregnant women,BMI>36kg/m2,The patients requiring GA due to inadequate effects, History of spine surgery in past and spine deformity.

A day before surgery, preanesthetic check up was done. A detailed history, thorough general physical and systematic examination was done followed by reviewing the investigations like HB, BT, CT, TLC, DLC, renal function test, liver function test, Blood sugar fasting, PTI, Urine R\E, ECG, Chest X-ray (PA view). Any special investigation if needed was ordered.After taking informed written consent from each patient, patient was kept fasting overnight. Tablet Rantidine 150 mg was given at bed time night before surgery. No sedative premedication was administered. The procedure of subarachnoid block was explained to the patients in detail. Patient was familiarized with Visual analogue score (VAS) and It was used for monitoring post operative pain.IV line was secured via 18 G cannula and RL infusion was started at the rate of 10ml/kg 20 min prior to surgery in preparation area.

After arrival of patient in Operation Theater, basic monitors NIBP, ECG, and SPO2 was attached and baseline parameters like Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), SPO2, Respiratory rate (RR) was noted. Using all aseptic precautions, in sitting position, L3-L4 interspace was identified. The skin and interspinous ligaments were infiltrated with 2ml of 2% lignocaine. Lumber puncture was performed in sitting position through mid line approach using 26G quincke needle. On ensuring the free CSF flow, study drug with total volume of 4.5ml [1% 2-chloroprocaine 4ml (40mg) +fentanyl 0.4ml (20μg) or 1% 2- chloroprocaine 4ml (40mg) + normal saline 0.4ml was administered slowly. After administering patient was placed supine. The drug combinations were prepared by the first an esthesiologist not involved in study. However, observations were made by the second anesthesiologist who was blinded to drug administered. HR, SBP, DBP, MAP, RR, SPO2 was recorded just after administering spinal anesthesia and it was labeled as 0 min. These parameters were recorded at 5 min, 10 min, 15 min, 20 min and then every 10 min till the end of

surgery and thereafter every 20 min till 3 hrs post operatively. Oxygen was supplemented to each patient and monitoring of SPO2 was done throughout the procedure.

The sensory level was assessed by loss of sensation using a blunt 25G hypodermic needle in caudal to cephalad direction and the grade of motor block was evaluated at 2, 4, 6, 8,10 and 15 min and thereafter at 15 min interval till the end of surgery and the motor block level was determined according to the Bromage Scale .During the tracking of the sensory block in patients, a maximum sensory block level, time to achieve maximum sensory block and the time for sensory block to regress to S2 dermatome was monitored. While tracking the motor block, time to achieve maximum degree of motor block and its regression to Bromage 0 was noted.

Arterial pressure ≥30% from baseline was initially treated with a rapid infusion of 200ml of RL solution. If this was not effective 3 mg ephedrine i/v increment was administered. Occurrence of clinically relevant bradycardia (defined as HR reduction <50bpm) was treated with increments of 0.3 mg atropine i/v. In post operative period if spo2 falls below 90%, oxygen (2-4 l/m) was administered via face mask. Respiratory depression was defined as respiratory rate less than 8 breath/min or spo2 <85%. Incidence of respiratory depression will be noted and treated accordingly. Nausea and pruritis was assessed on ordinal scale . Nausea with ordinal scale 2 and vomiting was treated with injection ondensatron 4mg IV. Shivering was treated with warm drapes and warm fluid. Duration of pain relieve was define as the time from spinal injection to first request for rescue analgesia or VAS<4 or whichever is earlier. IV injection of diclofenac sodium 75 mg in 100ml of NS was used as rescue analgesia.

Sedation was assessed according to Ramsay sedation score.The occurrence of transient neurological symptoms, PDPH and back pain was assessed 24 hrs and 7 days after surgery using a standardized study telephone call questionnaires asking patient in yes or no about paresthesias or dysesthesias in lower limbs or buttocks, headache and pain in back. The data so collected was analysed statistically. VAS score was monitored in post-operative period hourly after completion of surgery till 6th hour, subsequently 2 hourly till 12th hour then 3 hourly till completion of 24 hours. In the postoperative period, the time to first analgesic demand was noted and inj.diclofenac 75 mg was administered in patients with VAS>3. Patients were observed for any discomfort, nausea, vomiting, shivering, pruritus, bradycardia, and any other side-effects. All patients were observed in the post anesthesia care unit (PACU) and later in the ward. Severe pruritus and nausea/vomiting was treated with inj. chlorpheniramine maleate 10 mg and inj. Ondensetron 4 mg, respectively.

STATISTICALANALYSIS:

SPSS (version 16.0, SPSS Inc. Chicago, IL., USA) was used for statistical calculation. Data was expressed either as mean and standard deviation or number and percentage. Continuous variables age, BMI, duration of surgery, duration of sensory and motor blockade was compared using ANOVA test. P value of <0.05 was considered significant and <0.001 was considered highly significant. Paired and unpaired t-test and analysis of variance was used for statistical calculations. Categorical data was analysed using chi-square test.

OBSERVATIONS AND RESULTS

There was statistically no significant difference between the two groups with respect to the haemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure and SpO2. The two groups were also comparable in relation to age,height, weight, gender, duration of surgery and ASAstatus p-value > .05. (table 1, figure 1) The mean onset of maximum sensory block in CF group was 11.6 ± 1.99 min and that in CS group was 9.54 ±1.99 min. (p > 0.05) . The highest dermatomal level achieved in both groups was T 6. The mean time of sensory regression to S2 in CF group was 136 ±17 min. and that in the CS group was 99.86 ±10.55 min (p-value <0.0001). The mean time to achieve bromage 3 in CF group was 7.83 ± 1.54 min . and that in the CS group was 5.29±1.39 min., p-value >0.05. The mean time to achieve bromage 0 in CF group was 113.14±12.95 min and that in the CS group was 81.66±9.55min, p-value <0.001, indicating that the motor block was of shorter duration and was subject to rapid recovery in CS group as compared to CF group. The mean duration of sensory loss (total analgesia time) for CF group and CS group was 128 ± 8.94 min & 97.86±11.54 min., respectively (p=0.0001). Thus, we observed that sensory block lasted longer with CF group as compared with CS group. Three patient (8.6%) in the CF had hypotension (drop >25% SBP) as compared with one patient (2.8%) in the CS group and responded to inj. ephedrine, 6 mg along with IV fluids.Nausea/vomiting and shivering was experienced by one patient each in the CF group. Pruritus was present in two patients (8.6%) in the CF. They responded to inj. ondensetron, 4 mg, and inj. chlorpheniramine 10 mg, respectively. In the CF group, 15 patients (43%) had a sedation score of 1-2 as compared with 28 patients (80%) in the CS group who were calm and sleeping comfortably.

DISCUSSIONS AND CONCLUSIONS.

Spinal anaesthesia is the technique of choice of many anaesthesio logists for lower limb surgery because of its rapid onset, adequate motor and sensory blockade, long duration of action, minimal cardiovascular changes and adequate postoperative analgesia though for limited duration. Local anaesthetics are routinely injected solely intrathecally in spinal anaesthesia but various adjuvants to these agents have been used with purpose of improving the quality of subarachnoid block and enhancing the action of local anaesthetics. In recent years, use of intrathecal adjuvants had gained popularity with the aim of prolonging the duration of block, patient satisfaction, decreased resource utilization compared with general anaesthesia and faster recovery.

The current study found that the difference between the demographic profile including age, sex, height and weight of the patients in both the groups were statistically insignificant (p> 0.05).

In our study onset of sensory block was earlier in group CS it was 6.34±1.39 mins when compared with the group CF which was 7.83±0.79 mins and it was found to be statistically significant.

Gys B et al. done a study to compare Intrathecal prilocaine, 2–chloroprocaine,bupivacaine for ambulatory abdominal study herniorraphaphy. They found that mean time of onset of sensory block in 1% chloroprocaine group is 1.5 mins and bupivacaine group is 2.8 min. Tandan M et al[34] in their study they compared 2-chloroprocaine with bupivacaine and came to the conclusion that mean time of onset in both the group was 6 min. Our study also showed that time of onset of sensory block in group CS is 6.34±1.39 min. Time to reach bromage 2 and bromage 3 motor block We found that the mean time taken to reach bromage 2 motor block was early in the group CS i.e. 3.34 ± 1 mins than in group CF i.e. 5.11 ± 1.51 mins and this difference was statistically significant (p<0.05).Casati et al[7] compared 50mg of 2-chloroprocaine with 50mg of lidocaine and it was found that mean time of onset of motor block in chloroprocaine group is 8 mins and in lidocaine group is 12 mins. The difference was statistically significant as was in our study results.Our results matched with study done by Yoos JR et al, [41]who also found that mean time of onset of motor block was early in chloroprocaine group (40mg) as compare to bupivacaine (7.5mg) for ambulatory surgery. We found that the mean time taken to reach Bromage 3 motor block was5.29 ± 1.38 mins in group CS and 7.83 ± 1.58 mins in group CF. This difference was statistically significant (p<0.05). Singh G et al, [31] found that the mean time to achieve bromage 3 motor block was significantly delayed in group BF (bupivacaine 7.5mg +fentanyl 25µg) as compared to group BS (bupivacaine 7.5mg + saline), BC(bupivacaine 7.5mg + clonidine 75µg), BCF (bupivacvaine 7.5mg + fentanyl 712.5µg + clonidine 37.5µg). sharan R et al, [29] compared intrathecal clonidine and dexmedetomidine adjuvant to bupivacaine and reported that the time to achieve bromage 3 motor block was 15.36 ± 3.367 mins in bupivacaine group, 9.52 ± 1.876 mins in bupivacaine - clonidine group and 10.76 ± 1.744 mins in bupivacaine - dexmedetomidiine group. This difference between these was statistically significant as is in our study. Time to sensory regression to s2 dermatome (duration of sensory block) We noted the time taken for regression of the sensory blockade to S2 dermatome and this was labelled as duration of sensory block. In our study, we found that the mean time taken to reach sensory regression to S2 dermatome in group CS was 99.45± 12.98 mins and in group CF was123.86 ± 10.55 mins and the difference between the two mean values was statistically significant (p<0.05) i.e. Group CS showed a faster regression of the sensory block as compared to Group CF. Kouri ME et al, 21 calculated the time to regression of sensory block to S2 dermatome to be 103 ± 13 mins with 2-Chloroprocaine 40 mg as compared to 126 ± 16 mins with lidocaine 40 mg and the difference between these groups was statistically significant reflecting that sensory block with 2-chloroprocaine regressed early when compared with lidocaine. Vath J S et al, [38]) reported that the mean time

taken for regression to S2 dermatome was 104±7 mins in group 2-chloroprocaine with fentanyl and 95±9 mins in group 2-chloroprocaine with saline and the difference was statistically significant, showing that fentanyl when added to chloroprocaine prolongs the regression of block.Our results were similar to Ben david et al,[3] who found that block regression was significantly slower with addition of intrathecal fentanyl, as time to S2 regression were significantly slower in group 2 (buipvacaine + fentanyl) and the difference between these groups was statistically significant. Total duration of motor block (duration from onset of motor block i.e. bromage -3 to bromage 0).We observed that patients of group CF took longer time to reach modified bromage scale 0, which was 113.14 ± 12.95 mins as compared to group CS which was 81.66 ± 9.55 mins. Postoperatively, the resolution of the motor blockade was also monitored by asking the patient to move his lower limbs and the time taken to reach bromage 0 was noted. In our study, duration of motor block in group CS is 81.66 ± 9.5 mins, where as we observed the time to be 113.2 ± 12.95 mins in group CF. The difference in mean time to reach bromage 0 between the two groups was found to be statistically significant. Vaghadia H et al, [39] compared low dose 2% lidocaine (35mg) with 40 mg of 1% chloroprocaine, fentanyl (12.5µg) was used as adjuvant in both the group. It was found that motor recovery was same in both the group as fentanyl has minimal effect on motor blockade. Our study also confers that fentanyl as adjuvant to chloroprocaine has less effect on prolongation of motor block.

Vath J S and Kopacz D J , [20] compared the time to reach bromage 0 i.e. duration of motor block in chloroprocaine (40mg) with fentanyl or saline and found it to be 81 ± 16 mins and 67 ± 13 mins respectively and it was statistically significant. Lacasse MA et al, [23] who compared the same doses of 2-chloroprocaine and bupivacaine and found out that the time taken to reach bromage 0 was 76 mins and 119 mins respectively. The difference between the two groups was found to be statistically significant as was in our study. We found that time to first analgesic request was shorter in chloroprocaine with normal saline group than chloroprocaine with fentanyl group. The time of analgesic request in group CF was 128 ± 8.94 mins, 97.86 ±11.54 mins in group CS and difference was statistically significant.

Khezri MB et al, [19] done a comparative study and found that mean time to first analgesic request was significantly longer in adjuvant group as compared to bupivacaine group. Sharan R et al, [29]) compared different adjuvant with ropivacaine and found that the time to first analgesic request in adjuvant group was significantly longer as compared to ropivacaine group.

SIDE EFFECT

Postoperative vomiting was experienced by 2.86% of patients receiving 2-Chloroprocaine (40mg) with fentanyl (20µg) and it was treated by giving injection Ondansetron 4 mg i/v and whereas no case was reported in saline group. This difference was statistically insignificant. Our study was in accordance to Lacasse MA et al, [23] in which 4% patients in both 2-chloroprocaine and bupivacaine group complained of PONV. Also, similar results were found by Casati A et al, [6,7]) who found that 1 patient complained of nausea and vomiting in 2-Chloroprocaine(40mg) and 2 patients in chloroprocaine (30 mg) dose. This difference was statistically insignificant.

No patient in any group complained of TNS. Similar result was reported by Ben- David B et al, [3] as none of their patients complained of TNS like features. Our results were also consistent with those of Lacasse MA et al, [23] who found that 2% of his patients in both the 2-chloroprocaine (40 mg) and bupivacaine (7.5mg) group complained of TNS like symptoms but he could not confirm the diagnosis of TNS in them. In our study total 2 patients in chloroprocaine (40mg) with fentanyl (20µg) group had itching but no such case reported in saline group and also the difference was statistically insignificant.

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The present study shows Onset of sensory and motor block was found to be earlier in saline group as compared to fentanyl group and this difference was found to be statistically significant. Duration of sensory and motor block was again found to be prolonged in fentanyl group as compared to saline group with the results being statistically highly significant.We also found that time to first request for analgesia in postoperative period was earlier in saline group as compared to fentanyl group and it was found to be statistically significant. Some of the adverse effects noted in our study were nausea and vomiting, TNS and pruritis. However, none of adverse effects noted were found to be statistically significant in either group. There are only few studies in literature which have compared different adjuvants with chloroprocaine intrathecally. So, we planned to compare minimal dose of fentanyl as adjuvant required to achieve adequate subarachnoid block for lower limb surgeries.

Since offset of surgical anesthesia was shorter with minimal incidence of side effects on using combination of chloroprocaine and fentanyl intrathecally. We can recommend the use of fentanyl (20µg) with 1% 2- Chloroprocaine (40mg) for ambulatory surgeries with advantages of faster motor recovery and earlier hospital discharge when compared with chloroprocaine and saline intrathecally.

Tables and Figures

Table 1: Demographic Profile

Parameter	CF Group	CS Group	P value
Age	34.77±10.37	33.14±9.24	0.490
Height	156.09±6.13	156.49±6.26	0.818
Sex(M:F)	32:3	27:8	0.188
Weight	56.71±6.24	57.43±5.39	0.510

Table 2: Spinal Block Characteristics

Parameter	CF Group	CS Group	P value
Highest Sensory Level	T6	T6	>0.56
Time to Reach Peak Sensory level	11.6±1.90	9.54±1.99	=0.0001
Time regression to S2	136.17±12.98	99.86±10.55	<0.0001
Time to Reach bromage 3	7.83±1.54	5.29±1.39	<0.0001
Time to Reach bromage 0	113.14±12.94	81.66±9.95	<0.0001
Time to first request for Analgesia	128.14±8.94	97.86±11.54	<0.0001

Table 3: Side effect Profile

Parameter	CF Group	CS Group	P value
Hypotension	2	1	0.521
Bradycardia	1	0	0.240
Nausea/Vomiting	1	0	0.240
Respiratory Depression	0	0	1.000
Shivering	1	0	1.000
Pruritis	3	0	0.092

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