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Original Article

Comparison of Efficacy of Intrathecal 2-Chloroprocaine and 2-Chloroprocaine with Fentanyl in Perianal Surgery: A Randomized Control Study

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Abstract

Background: Spinal anesthesia is considered a reliable and safe technique for perianal surgeries. The revival of older local anesthetics, such as 2-Chloroprocaine (CP) a short acting amino ester has been successfully used for spinal anesthesia in ambulatory setting. The addition of intrathecal opioids as adjuvants has been well proven to improve the quality of spinal anesthesia and prolong the duration of analgesia.

Aim: This study is aimed to evaluate and compare efficacy of spinal anesthesia and recovery profile using 2-CP and fentanyl as an adjuvant to 2-CP in elective perianal surgeries.

Materials and Methods: This prospective, randomized, and comparative study included 90 adult patients planned perianal surgeries with subarachnoid block. These patients were categorised into two groups and administered 30 mg of 2-CP and 0.4 ml normal saline intrathecally (Group A) or 30 mg of 2-CP and 0.4 ml (20 μg) fentanyl (Group B) intrathecally.

Results: A clinically significant difference in the meantime for sensory regression to L1 between two groups ($P < 0.001$) was witnessed in the study. The mean systolic blood pressure of Group A compared to Group B was lower and was statistically significant. With ($P < 0.0001$) between the two groups, there was statistical significance in the requirement of first rescue analgesia. There was no significant difference between groups in the intraoperative parameters of sensory and motor characteristics, including meantime to readiness for surgery, time to achieve peak sensory block.

Conclusion: The addition of fentanyl (20 mcg) to 2-CP (30 mg) has clinical value as it improved the quality of the block with a superior analgesic effect. In addition, it is an effective combination with a favorable recovery profile and immediate eligibility for home discharge compared with intrathecal 2-CP.

Key words: Adjuvants, Early discharge, Fentanyl, 2-chloroprocaine

INTRODUCTION

In daycare surgeries, spinal anesthesia is reliable, safe, and provides adequate analgesic effect but delayed ambulation and risk of urinary retention limit its use.[1] Recently, the revival of older local anesthetics such as 2-Chloroprocaine (CP) offers a solution for a search of ideal agents in the modern ambulatory setting.[2]

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Local anesthesia is the chemical compound capable of reversibly inhibiting the propagation of impulses in nerve cells. Based on the link between the aromatic portion and the intermediate hydrocarbon chain, the amino ester group has an ester linkage, while the amino amides have an amide link.

Low doses of long-acting local anesthetics such as bupivacaine, ropivacaine, and levobupivacaine are commonly administered intrathecally. However, they cause

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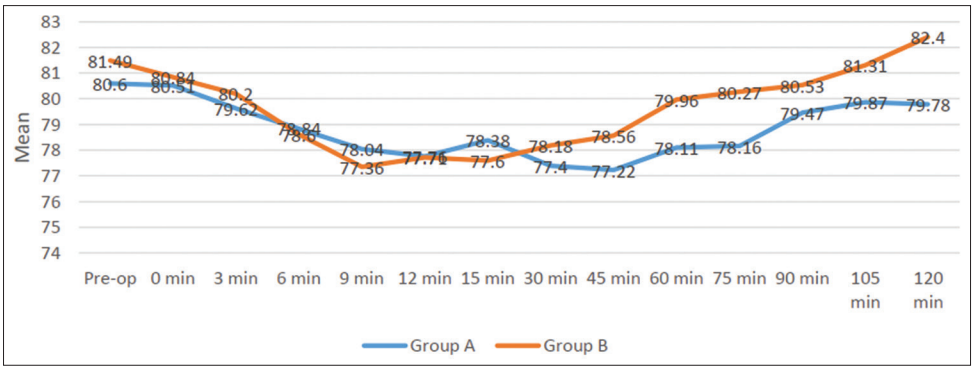

Figure 1: Mean pulse rate in the two groups

considerable delay in recovery, hospital discharge with lower block efficacy.[3]

2-CP, an amino ester local anesthetic, has been successfully used for spinal anesthesia since 1952.[4] In the early 1980s, it was withdrawn from commercial use due to concerns regarding neurotoxicity following accidental intrathecal injection during epidural labor analgesia.[5]

In recent studies, the preservative-free 2-CP seems to be a predictable drug with a good recovery profile and has generated interest among clinicians working in fast-paced ambulatory surgical settings.[6] 2-CP has advantages of quick onset and short duration of action. Plain 2-CP 1% free of both antioxidants and preservatives was introduced in 2004 and is less toxic than other local anesthetics. 2-CP has a rapid onset of action of 5–10 min because of its high tissue penetrance. The duration of the block is dose-dependent, with complete resolution of sensory block after 70–150 min with 30–60 mg.

The recent trend in ambulatory surgery is to administer a lower dose of local anesthetic with adjuvants such as opioids to provide segmental block; opioids create a synergistic effect by acting directly on opioid receptors in the spinal cord. The addition of intrathecal opioids as adjuvants improves the quality of spinal anesthesia and prolongs the duration of analgesia. Fentanyl is a synthetic opioid agonist which is 15–125 times more potent than morphine.

Fentanyl has pure agonist action on stereotypic μ type opioid receptors and can also bind to delta and kappa receptors with low affinity. It is very highly lipophilic, so it easily crosses the blood-brain barrier, decreases neurotransmission, and has a rapid onset of action with greater potency. Fentanyl has been proven to be a safe drug that enhances the analgesic effect when administered intrathecally. Fentanyl injected intrathecally would display moderate spinal selectivity, that is, provide the benefit of analgesia at the spinal level without the problems of respiratory depression at the systemic level.

Our study outcome was to estimate the onset and duration of sensory and motor blockade, evaluate the hemodynamic alteration, and estimate the time to reach eligibility for discharge from hospital if given in combination with opioid fentanyl.

MATERIALS AND METHODS

This prospective, randomized, and clinical study included that 90 patients (45 in each group) scheduled to undergo perianal surgeries were conducted at Government Villupuram Medical College. After being duly approved by the Institutional Ethics Committee, patients were enrolled after receiving informed consent between December 2019 and August 2020.

Patients with the American Society of Anesthesiologists physical status Class I and Class II of either sex, age between 18 and 60 years, weighing between 50 and 70 kg, and willing to participate were included in the study.

Patients with American Society of Anesthesiologists physical status Class III and Class IV aged above 18 years with a clinical condition such as any coagulopathy, taking anticoagulants therapy, neurological and musculoskeletal disorder, skin infection at lumbar area, allergy, or intolerance to local anesthetic were not willing to participate in the study and were excluded from the study.

Pre-anesthetic evaluation included, details (associated comorbidities, previous surgeries, medication, and drug allergy) were noted. General examination of height, weight, pulse rate, blood pressure (BP), oxygen saturation, and routine baseline investigations such as complete blood count, blood urea nitrogen and serum creatinine, random blood sugar, electrocardiogram, and chest X-ray was carried out. The anesthetic procedure was standardized for all patients, wherein they were instructed to overnight fasting for 6 h.

The patient was shifted to OT and baseline vital parameters were recorded. Then, intravenous access was secured using an 18G cannula and preloading was done with Ringer Lactate at 10 ml/kg.

After skin sterilization with betadine, the skin was infiltrated with 2% lignocaine in the L3-L4 interspace. Using 27G, Quincke's needle subarachnoid block was performed. The drug was injected as per the randomization group:

- GROUP A – 30 mg (3 ml) of 2-CP and 0.4 ml normal saline intrathecally
- GROUP B – 30 mg (3 ml) of 2-CP and 0.4 ml (20 µg) fentanyl intrathecally.

After completing the spinal injection, the patients were immediately placed in a supine position. After 5 min, the patients were put in the lithotomy position. Hemodynamic variables were recorded every 3 min for the first 15 min then every 5 min for the next 30 min and every 15 min for 120 min. Hypotension was treated with injection ephedrine 3 mg IV in incremental doses if systolic BP falls >20% from the baseline value. Bradycardia was treated if heart rate <50 beats/min with injection atropine 0.6 mg IV. Sensory and motor blockade was recorded for every 3 min during the initial 15 min period and after the surgical procedure. The time of completion of spinal drug injection was considered as zero time. The sensory level of the block was assessed in a caudal to cephalad direction by pinprick sensation using a 22Gsterile needle.

The time to readiness for surgery was assessed as the time interval between local anesthetic injection and the onset of complete loss of pinprick sensation in the anterior axillary bilaterally at T10 level. Other parameters observed were maximum sensory block height reached; time to reach maximum block height, time taken for regression to L1, time taken for complete regression of sensory block, time to ambulation, time to micturition, and time to eligibility for discharge from hospital were also recorded post-operation.

Statistical Analysis

The Chi-square test was used as a test of significance for qualitative data. An independent *t*-test was used as a test of significance between quantitative variables. $P < 0.05$ was considered statistically significant.

Statistical Software

MS Excel and Statistical Package for the Social Sciences version 22 (IBM SPSS Statistics, Somers NY, USA) were used to analyze data.

RESULTS

The demographic profile of patients in Groups A and B varied from 19 years to 53 and 55, respectively, as shown in Table 1. However, the distribution of patients across the age group was not significant ($P > 0.5$).

The Chi-square test shows no significant difference between the groups for males and females. ($P = 0.058$) as shown in the graph. The independent' *t*-test results revealed no significant difference in mean height ($P = 0.183$) and weight ($P = 0.643$) for the comparable groups.

The different types of surgical procedures were used in the study, showing no significant difference between the groups ($P = 0.337$).

The *P*-value of American Society of Anesthesiologists (ASA) physical status was 0.830, which was also statistically not significant. Although there was no significant difference in pulse rate, diastolic BP was noted between the two groups in the intra-operative and post-operative periods. The mean systolic BP of Group A compared to Group B was lower and statistically significant ($P = 0.016$) at 105 min intervals [Figures 1-4].

Five patients (11.1%) in Group A and two patients (4.4%) in Group B developed hypotension. One patient (2.2%) in Group B developed bradycardia with hypotension and treated with Atropine and Ephedrine. The Chi-square test shows no significant difference between the groups concerning complications [Figure 4].

There was no significant difference between groups in the meantime to readiness for surgery, time to achieve peak

Table 1: Distribution of patients characteristics

Patient's characteristics	Group A	Group B	*P*-value
Age	35.08±9.29	36.42±9.37	0.474
Height	161.68±4.97	160.2±5.5	0.183
Weight	67.82±8.37	66.93±9.7	0.643

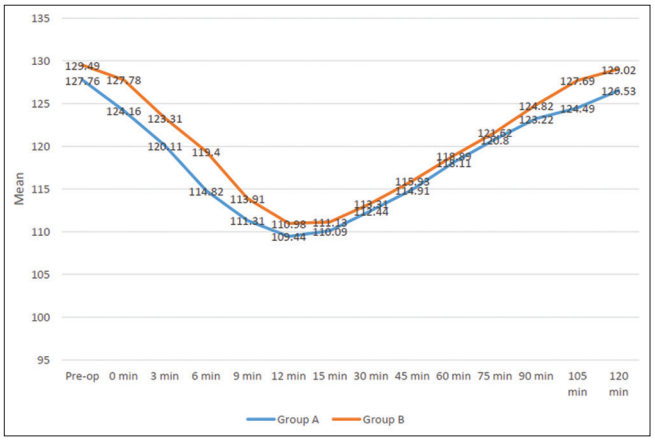

Figure 2: Mean systolic blood pressure in the two groups

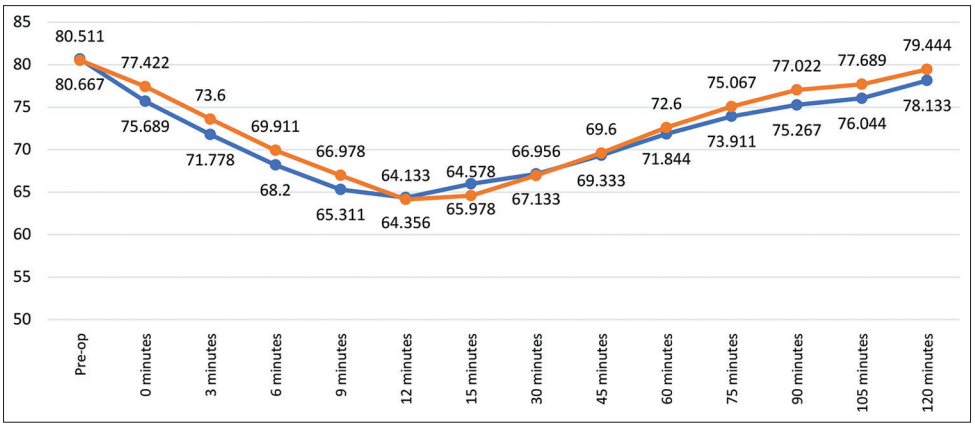

Figure 3: Mean comparison of diastolic blood pressure in the two groups

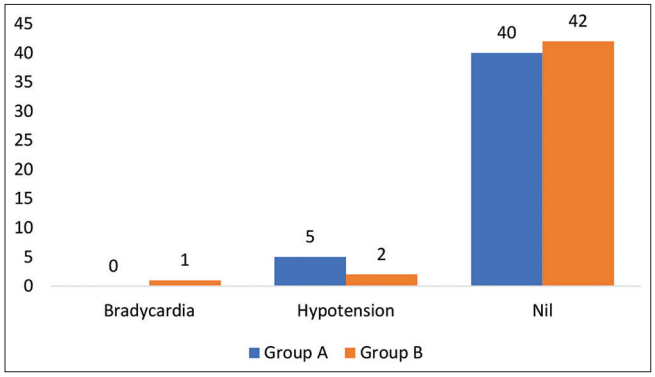

Figure 4: Distribution of complications

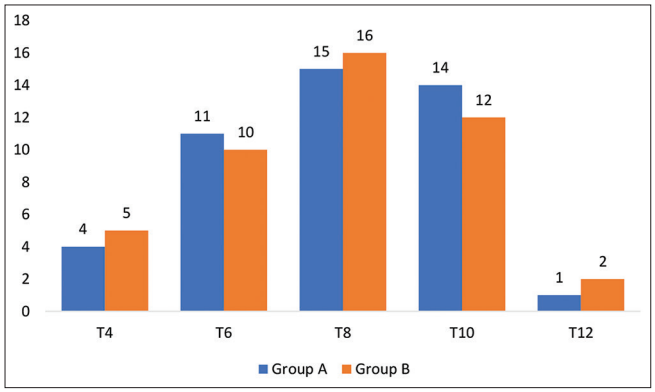

Figure 5: Maximum level of sensory block attained in two groups

sensory block, peak motor block, and time to reach motor block score of 4 [Table 2].

Group B had slower sensory regression to L1 than Group A and a clinically significant difference in the meantime for sensory regression to L1 between the two groups ($P < 0.001$). Regarding the duration of the sensory blockade and motor blockade, $P < 0.0001$ compared between two clinically significant groups. Group B had a longer sensory block and motor block duration than Group A [Figure 5 and Table 3].

In Group A, mean duration of requested rescue analgesia was 90.2 ± 8.2 min compared to Group B 125.44 ± 9.7 min with $P < 0.0001$, which was statistically significant.

The post-operative nausea and vomiting incidences were 4.4% and 2.1% in Groups A and B, respectively. The incidence of Pruritis in Group B was 55.6%, and there was no case in Group A, revealing a highly significant difference with $P < 0.001$. The mean time to ambulation in Group A and Group B was statistically significant with $P = 0.022$. The observed mean time for voiding in Group A compared to Group B was statistically significant with $P = 0.017$.

The observed mean time to reach eligibility for home discharge was almost similar in both groups (205.7 ± 13 min vs. 200.5 ± 12 min) with no clinically significant difference noted between Group A and Group B.

DISCUSSION

In the study by Schmittner *et al.*, spinal anesthesia is superior to total intravenous anesthesia in patients undergoing perianal surgery in terms of analgesic requirements and post-operative recovery.[7] The most of the perianal surgeries are short duration, to improve the perioperative efficiency, the intrathecal agent should provide rapid recovery with effective discharge time. One of the aminoester is 2-CP, with a short half-life of 40 min. Free of both antioxidants and preservatives, it was reintroduced in the market after being withdrawn due to neurotoxicity concerns. It fulfills the key criteria of an ideal intrathecal agent for ambulatory surgery.[8] 2-CP has a faster offset of action, leading to early post-operative pain, which is important in determining safe discharge. Intrathecal opioids provide effective analgesia in the post-operative period. Fentanyl, a short-acting lipophilic opioid, stimulates μ1 and μ2 receptors potentiating the afferent sensory blockade without prolonging recovery and facilitating a reduction in local anesthetic dose.[9] This study

Table 2: Distribution of intraoperative parameters

Intra operative parameters	Group A	Group B	*P*-value
Time to readiness for surgery	4.2±1.74	4.867±1.949	0.091
Time to achieve peak sensory block	6.6±1.763	7.267±1.75	0.075
Peak motor block achieved by Modified Bromage Scale	3.956±0.208	3.889±0.318	0.242
Time to reach motor block score of 4	4±1.43	4.533±1.517	0.09

Table 3: Distribution sensory and motor blockade

Patient's characteristics	Group A	Group B	*P*-value
Sensory regression to L1	59.66±6.6	72.77±8.56	<0.0001
Duration of sensory block	83.77±8.53	103.77±7.39	<0.0001
Duration of motor block	68.77±7.62	83.11±7.7	<0.0001
Duration of analgesia	90.22±8.25	125.44±9.76	<0.0001

was a prospective, randomized, and double-blinded clinical study. In our study, no statistically significant difference was found in both groups compared to age, sex, height, weight, ASA physical status, duration, and type of surgery. Based on the previous clinical studies observation, considering the type and duration of surgical procedure, in our study, we decided to perform spinal anesthesia in a sitting position with 30 mg of 2-CP in both groups.

Our study found that the meantime for surgery readiness (at T10) in both groups was not statistically significant. We observed faster onset than the time observed in the study done by Lacasse *et al.* (6 min).[10] Peak block height with relation to the height of patients was comparable. In Group A 8.9%, 24.4%, 33.3%, and 31.1% whereas in Group B 11.1%, 22.2%, 33.3%, and 26.7%, people achieved a peak block height of T4, T6, T8, and T10, respectively. The sensory level blockade T8 was noted in patients of both groups (33.3% vs. 33.3%).

In the study by Vath and Kopacz,[11] peak block height reached T3 level in the fentanyl group, which was higher compared to our study due to the low dose of 2-CP used in our study. In studies conducted by Bhaskara *et al.*[12] and Siddaiah *et al.*[13] with fentanyl as an adjuvant to 2-CP, the maximum level of sensory blockade observed was T8 with no statistical significance concurs with our study. In our study, the addition of intrathecal fentanyl resulted in prolongation of sensory blockade, as demonstrated by delay in time to L1 regression and complete sensory regression.

In our study, fentanyl significantly prolonged the post-operative analgesia by 1.65 times compared to another group. A significant prolongation of sensory and motor blockade by adding fentanyl to 2-CP was observed by Vaghadia *et al.*,[14] which was similar to our study. Our results were similar to the studies wherein Vath and Kopacz[11] used 20 μg of fentanyl with 2-CP, and Davis and Kopacz[15] added 15 μg of clonidine to 30 mg of 2-CP.

No dissimilarity was observed in both groups' quality and motor block onset. Yet, the duration of motor blockade was prolonged by 15 min in Group B. Indeed, adjuvants such as opioids remarkably minimize the complication by reducing the dose of local anesthesia. Our study patients neither developed desaturation nor apnea due to respiratory depression. A previous study found that 25 μg of intrathecal fentanyl was well tolerated in the elderly, but the incidence of respiratory depression has an increasing trend with a dose of 40–50 μg. Thus, our dose of fentanyl 20 μg is unlikely to cause respiratory depression.[16]

Our finding suggests that the addition of fentanyl (20 mcg) to 2-CP (30 mg) has clinical value as it improved the quality of the block with a superior analgesic effect. Furthermore, it is an effective combination with a favorable recovery profile and prompt eligibility for home discharge.

In our study, there was no remarkable difference in the time of voiding between the two groups but statistically significant compared to the study of Liu *et al.*,[17] where the meantime of voiding was not prolonged with the addition of a small dose of intrathecal fentanyl. Our data demonstrated that the time to void was shorter, and the incidence of urinary retention is negligible in the Fentanyl group. This effect might be explained by the fact that fentanyl decreases bladder compliance and causes relaxation of the internal urethral sphincter due to the potent inhibitory effect.

CONCLUSION

Our finding suggests that the addition of fentanyl (20 mcg) to 2-CP (30 mg) has clinical value as it improved the quality of the block with a superior analgesic effect. Furthermore, it is an effective combination with a favorable recovery profile and prompt eligibility for home discharge.

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