Original Article

Intrathecal 1% 2-chlorprocaine for short gynecological day care procedures: Prospective, randomized, dose finding study

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Abstract

Background and Aims: Establishing the optimum dose of intrathecal 1% 2-chlorprocaine may reduce the discharge time and encourage more widespread use of spinal anesthesia for day care procedures. The aim of this study was to compare the efficacy and recovery characteristics of three different doses of intrathecal 1% 2-chlorprocaine for short gynecological day care procedures.

Material and Methods: Fifty-one patients scheduled for elective day care gynecological procedures lasting less than 60 min and were randomly divided into three groups of 17 each to receive 35 mg, 40 mg, or 45 mg intrathecal 1% 2-chlorprocaine. Demographic data, time required to achieve readiness for surgery, time required to attain discharge criteria, maximum block height achieved, and adverse effects were recorded in each group.

Results: The time required to achieve readiness for surgery was similar between the three groups ($P = 0.306$). However, 35 mg group required the shortest time to ambulate and there was a significant difference as compared with both 40 mg ($P = 0.012$) and 45 mg ($P = 0.001$). Voiding and the fulfillment of the discharge parameters were also attained more rapidly in the 35 mg group [133 (120,155) min] as compared with both 40 mg [164 (145,175) min, $P = 0.000$] and 45 mg [160 (150,175) min, $P = 0.000$]. None of the patients reported neurological symptoms during the follow-up.

Conclusion: The 35 mg intrathecal 1% 2-chlorprocaine not only provides reliable anesthesia for short gynecological procedures but also facilitates faster achievement of the discharge parameters as compared with the 40 mg and 45 mg doses.

Keywords: 1% 2-Chlorprocaine, ambulatory surgery, gynecological day care procedures, modified PADSS

Introduction

Ideal local anesthetic for the day care procedures must exhibit rapid onset, rapid regression of the motor and sensory block, and minimum side effects. Lidocaine, procaine, and 1% 2-chlorprocaine fulfill these key pharmacokinetic criteria. However, lidocaine was abandoned due to the reports of transient neurological symptoms (TNS),[1,2] whereas procaine was associated with high rate of inadequate block, neurotoxicity, and intraoperative nausea.[3] Similarly, there were several reports of neurotoxicity with 2-chlorprocaine, attributed either to the preservative bisulfite or higher doses of the local anesthetic itself.[4] However, the preservative free formulation of 1% 2-chlorprocaine has been used as an effective alternative without any concerns of TNSs.[5]

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1% 2-chlorprocaine has been found to be effective in doses between 30 mg and 60 mg for procedures lasting 45 to 60 min in several dose-finding studies.[6] Its minimum effective dose for the outpatient perianal surgeries and lower limb procedures has been investigated in the past.[7,8] However, literature lacks evidence regarding the most suitable dose for gynecological day care procedures, which require comparatively higher levels of block (T10). We therefore conducted this study to evaluate the efficacy and recovery time required after administration of its three different doses, that is, 35, 40, and 45 mg for various gynecological outpatient procedures.

The primary outcome of this study was the time from spinal anesthesia to the time required to attain the discharge criteria assessed according to the modified post anesthetic discharge scoring system (modified PADSS).[9] The secondary outcome included the time to readiness for the surgery, time required for complete regression of block, maximum block height attained, value of modified PADSS at the time of discharge, the hemodynamic parameters, and adverse effects if any.

Material and Methods

This prospective, randomized, parallel group, observer blinded study was conducted between September 2019 to August 2020 after obtaining clearance from the institutional ethics committee [CREC/2019/Aug/1(iii)]. This study is registered with clinical trials registry of India as CTRI/2019/11022025. After obtaining a written informed consent 51 ASA I–II patients, 18 to 60 years of age, weighing between 50 and 80 kg, scheduled for short gynecological day care procedures such as hysteroscopy, vulval or vaginal or endometrial biopsy, cystocele repair, dilatation, and evacuation or curettage, lasting less than 60 mins were enrolled for the study. The exclusion criteria from the study were any known contraindication to spinal anesthesia, allergy to local anesthetics, severe cardiopulmonary or renal diseases, or significant neurological disorders.

The patients and the observer recording the outcome measure were blinded to the group allocation. The unblinded anesthesia provider randomly allocated patients into three groups of 17 each using a computer-generated randomization sequence. The allocation ratio was 1:1:1. According to the group allotment patients received three different doses of 1% 2-chlorprocaine: 35 mg, 40 mg, or 45 mg.

Anesthetic technique

After arriving in the operation theater, standard ASA monitors including ECG, noninvasive blood pressure, and pulse oximeter were applied to each patient; 18G IV cannula was secured and Ringer's lactate solution infusion was started. Spinal anesthesia was performed in the sitting position in L3-4 or L2-3 interspace using 25G or 27G Whitacre spinal needle. The consultant anesthesiologist injected the dose of the drug as per the randomization table. After administration of spinal anesthesia, patients were placed in supine position. A blinded observer assessed sensory and motor block every 3 mins till the readiness for surgery was achieved. Sensory level was assessed using loss of pinprick sensation. Motor power was checked using modified Bromage scale (0 = no motor block, full straight leg raise possible; 1 = ability to flex knee, inability to raise extended legs; 2 = inability to flex knees, 3 = inability to dorsiflex the foot). Readiness for surgery was defined as loss of pinprick sensation at T 10 dermatome with a modified Bromagescore ≥2. After achieving the readiness for surgery, criteria patient was placed in the lithotomy position and sensory level was assessed every 15 min during the first 60 min to identify the maximum block height reached. After 60 min, sensory and motor block were assessed every 30 min till the discharge criteria was met. If the patient complained of pain intraoperatively, fentanyl was given in bolus doses of 25 μg upto a maximum of 2 μg/kg. If pain or discomfort persisted, general anesthesia was administered. The fentanyl requirement in each group was noted.

Cardiorespiratory parameters such as heart rate, noninvasive blood pressure, and oxygen saturation were recorded at baseline, immediately after the administration of spinal anesthesia, every 5 min for the first 30 min, and every 15 min thereafter till the discharge criteria were met. Clinically significant bradycardia was defined as HR ≤45/min and was treated with 0.6 mg IV atropine. Systolic arterial BP ≤30% from baseline was considered as clinically relevant and treated with rapid bolus of Ringer's lactate and bolus doses of Phenylephrine.[10]

Each patient received oral diclofenac 75 mg twice daily starting from the morning of the procedure and 1 gm paracetamol IV intaoperatively. Injection tramadol was administered as rescue analgesic in a dose of 1.5 mg/kg if patient complained of pain or VAS was recorded more than 4 in the recovery room.

The time required for complete regression of the block, the time required for ambulation, and voiding were recorded by the blinded observer in the PACU (Post anesthesia care unit). The time required to attain the discharge criteria, was defined as the time from administration of spinal anesthesia to the time required to fulfill modified PADSS. This scoring system consists of 6 characteristics including vital signs, ambulation, PONV (Post operative nausea and vomiting), pain, surgical bleeding, and voiding. The score for each criteria ranges from 0 to 2. To fulfill this criteria, vital sign score must be 2 and the value for all other criteria must

be >0.[9] Twenty-four hours after the discharge, each patient was followed-up over the telephone to identify adverse events such as nausea, vomiting, headache, backache, and difficulty in voiding or neurological symptoms such as back ache and paresthesia.

Sample size calculation and statistical analysis

A sample size of 15 patients in each group was found to be sufficient to detect a difference of 15 min in the time required to void with a power of 80% and a significance level of 1%. The value of standard deviation was assumed to be 21 based on a previous study.[6] Considering a drop out rate of 10%, the sample size was extended to 17 patients in each group. The continuous variables were expressed as mean ± SD and categorical variables as numbers and percentage. The time related and discharge score related variables were represented as median (max, min). The nonparametric statistical test of Kruskal–Wallis was used analyze the data in the three groups. Mann–Whitney test was used to analyze the data to detect the difference between various groups. *P* value of less than 0.05 was considered statistically significant. SPSS Inc 2009, PASW Statistics for Windows, Version 18.0, Chicago: SPSS Inc were used for all statistical analysis.

Results

A total of 51 patients were enrolled and each patient completed the study [Figure 1]. The three groups were similar in terms of various demographic variables such as age, height, weight, and ASA physical status. The duration of surgery was also comparable between the three groups ($P = 0.490$) [Table 1].

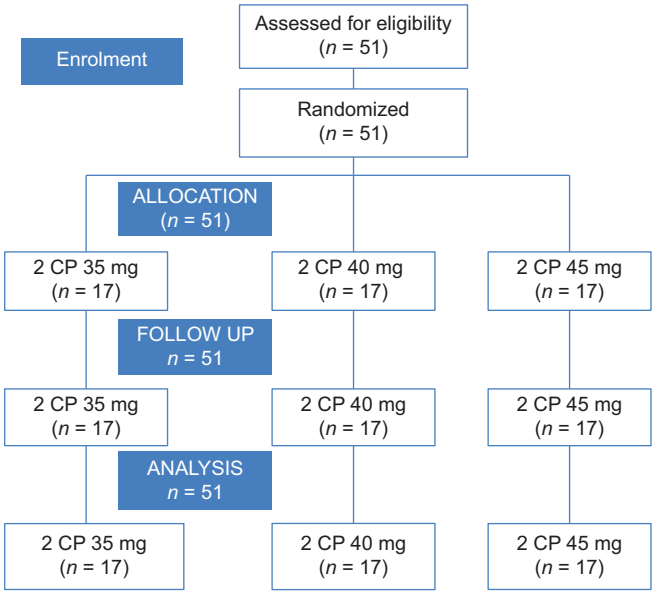

Figure 1: Consort Flow Diagram for allocation, follow-up, and analysis of patients

We recorded the time required to achieve the discharge criteria as 133 (120,155), 164 (145,175), 160 (150,175) min in 35, 40, and 45 mg groups, respectively. Comparing these variables in between the groups revealed significantly shorter time in 35 mg group as compared with both 40 mg ($P = 0.000$) and 45 mg ($P = 0.000$) groups [Table 2].

Amongst the six variables of mPADSS, voiding was the last criteria to be fulfilled and in all patients voiding time was same as the discharge time. Compared with the 35 mg group, 40 and 45 mg had significantly prolonged voiding time. However, one patient in 35 mg group recorded prolonged voiding time of 155 min similar to 40 and 45 mg groups, whereas another subject in the 40 mg group recorded shorter voiding time of 145 min comparable to 35 mg group [Figure 2]. The ambulation time was recorded as 118 (102,132), 128 (110,142), and 129 (118,142) min for 35, 40, and 45 mg groups, respectively, and was achieved much earlier in 35 mg group as compared with both 40 mg ($P = 0.012$) and 45 mg ($P = 0.001$) groups [Table 2]. Two subjects in the 40 mg group recorded exceptionally shorter time to ambulate, that is, 110 and 112 min, respectively, whereas one subject required 142 min to ambulate, which was similar to the 45 mg

Table 1: Patient characteristics

	35 mg	40 mg	45 mg	*P*
Age (years)	44.18±9.416	39.47±10.754	42±11.916	0.226
Height (m)	159.24±3.345	161.65±4.182	162.06±3.733	0.068
Weight (Kg)	61.71±4.909	65.06±6.015	63.06±5.847	0.292
ASA I/II (N)	13/4	14/3	12/5	0.721
Duration of surgery (min)	33.65±6.480	36.29±6.293	34.65±5.590	0.490

Values expressed as mean±SD or numbers, ASA: American Society of Anesthesiologist

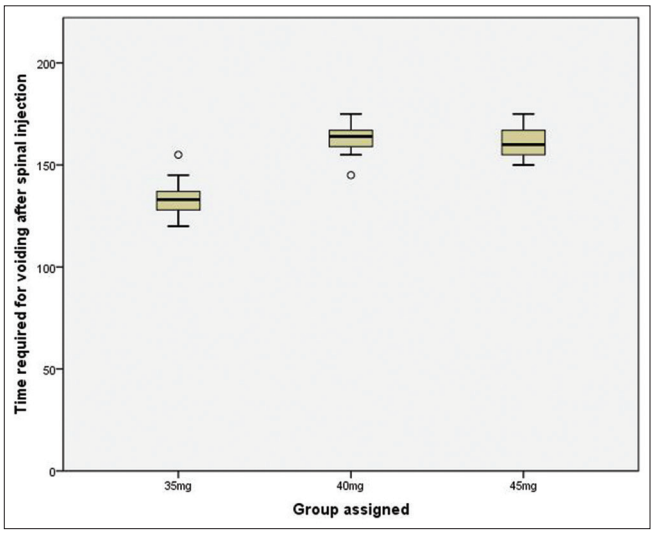

Figure 2: Boxplots for time required for voiding and discharge. The inner horizontal line within the box represents the median time and the horizontal lines of the whiskers represent the minimum and maximum time

group [Figure 3]. Other four variables of the discharge score, that is, vital signs, postoperative pain, PONV, and surgical bleeding were comparable between the three groups. After administration of spinal anesthesia, one patient in 35 mg, and two in 45 mg group recorded hypotension, which responded to the fluid bolus and intravenous phenylephrine.

There was no significant difference in the time required for the readiness for surgery between the three groups ($P = 0.306$) [Table 2, Figure 4]. Spinal anesthesia was successful in all patients and none required conversion to general anesthesia. Only one patient in the 40 mg group required 25 μg fentanyl intraoperatively. The peak block height attained was T7, T4, and T2 in the 35, 40, and 45 mg groups, respectively [Figure 5]. The difference in the median time required for complete regression of the block was significantly lower in the 35 mg group as compared with 45 mg groups ($P = 0.027$) [Table 2]. There was no significant difference between the three groups in the median values recorded for modified PADSS at the time of discharge ($P = 0.996$) [Table 2].

Table 2: Comparative data recorded in the three groups

	35 mg	40 mg	45 mg	*P*
Time for readiness for surgery (min)	7 (4,11)	6 (4,9)	7 (5,8)	0.306
Maximum block height	T8 (17.6%)	T4 (17.6%)	T2 (5.89%)	
Time for complete regression of block (min)	100 (90, 120)	99 (93, 110)	109.5 (99,129)	35vs40=0.367 35vs 45=0.027*
Time for ambulation (min)	118 (102, 132)	128 (110, 142)	129 (118, 142)	35 vs 40=0.012* 35vs 45=0.001*
Time for voiding (min)	133 (120, 155)	164 (145, 175)	160 (150, 175)	35 vs 40=0.000* 35 vs 45=0.000*
Discharge time	133 (120, 155)	164 (145, 175)	160 (150, 175)	35 vs 40=0.000* 35 vs 45=0.000*
Modified PADSS	12 (11,12)	12 (11,12)	12 (10,12)	0.996

*Values expressed as median (min, max), *P<0.05 statistically significant, PADSS: post anesthetic discharge scoring system*

The incidence of postoperative complications was low and statistically insignificant between the three groups. None of the patients complained of neurological symptoms or backache during the follow-up and only one patient in the 40 mg group developed mild postdural puncture headache, which responded well to conservative management and NSAIDs.

Discussion

Spinal anesthesia offers several advantages in the day care setting.[11,12] One of the prerequisites for conducting gynecological procedures under spinal anesthesia is the achievement of block height upto T 10. It is therefore very important to select the lowest dose of the local anesthetic, which provides reliable block height and early recovery at the same time.

In our study, we observed that recovery time was similar with 40 and 45 mg doses but it was significantly shorter with 35 mg. In agreement with our study, Ghisi *et al.* recorded significantly faster achievement of unassisted ambulation and voiding with 30 mg dose in a study conducted on patients undergoing lower limb procedures.[8] Whereas the time required to achieve these recovery parameters was much prolonged and almost similar with 40 and 50 mg doses. In contrast, Smith *et al.* observed a dose dependent prolongation of the recovery parameters in a study conducted on the volunteers.[6] These different findings may be explained by the fact that the dose

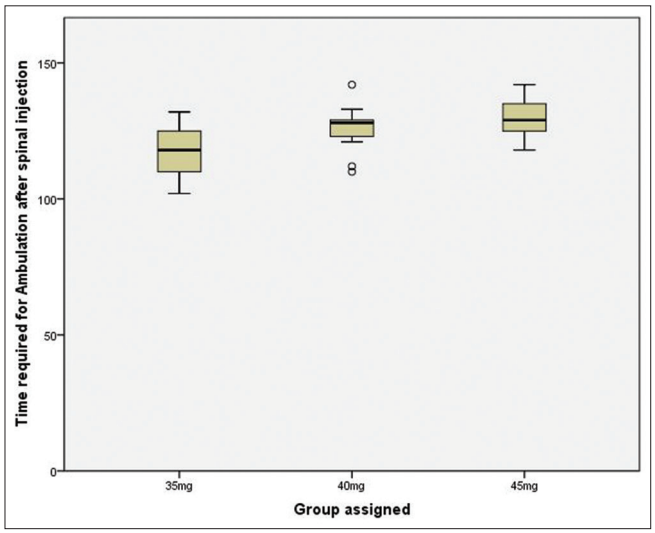

Figure 3: Boxplots for time required for ambulation. The inner horizontal line within the box represents the median time and the horizontal lines of the whiskers represent the minimum and maximum time

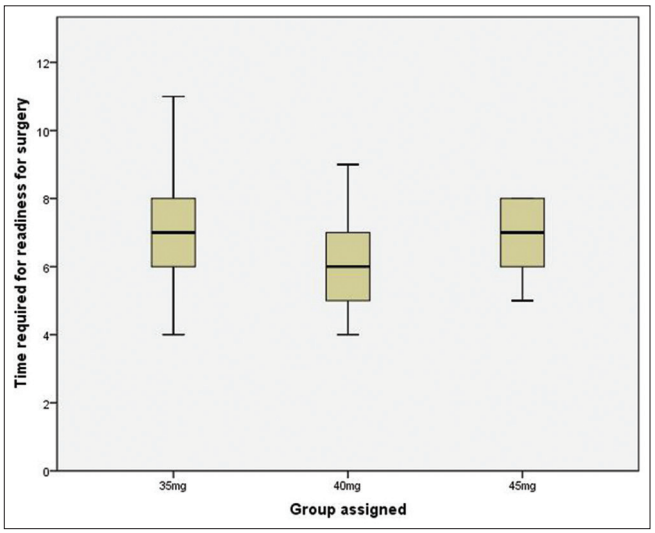

Figure 4: Boxplots for time required to attain readiness for surgery. The inner horizontal line within the box represents the median time and the horizontal lines of the whiskers represent the minimum and maximum time

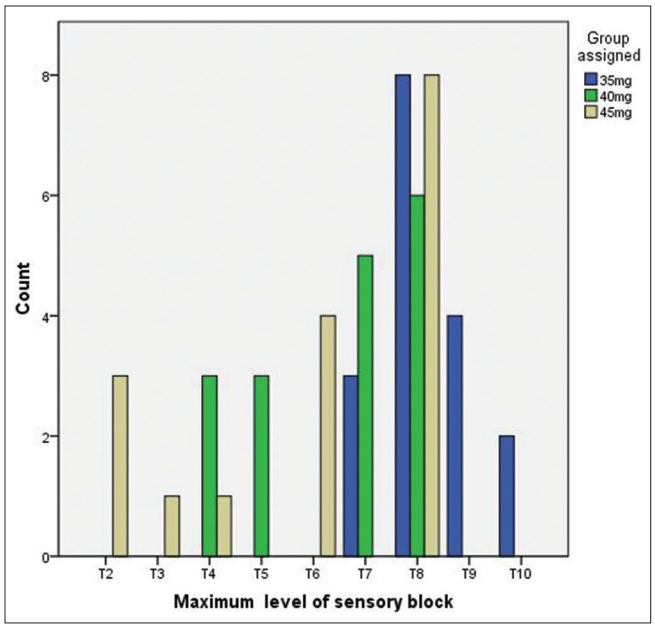

Figure 5: Comparison of the maximum block height attained in the three groups

dependent prolongation of the discharge variables is more likely to manifest with higher dose difference between the study groups. Smith *et al.* used a dose difference of 15 mg between the two groups (30 mg vs 45 mg vs 60 mg) as compared with 5 mg (35 mg vs 40 mg vs 45 mg) used in our study. The purpose of using a small dose difference in our study was to identify the lowest effective dose. Early recovery from the effects of spinal anesthesia may provide several benefits such as improved patient comfort, reduced hemodynamic changes, early mobilization, less PONV, and efficient utilization of PACU staff and resources.[5]

Past studies have documented that 30 mg dose produces less motor block, sacral sparing, and sensory anesthesia suitable only for brief procedures.[13] Therefore, we used 35 mg as the lowest dose and selected further doses in increments of 5 mg. None of the patients required conversion to general anesthesia and the intraoperative fentanyl requirement was minimal. Rattenberry *et al.*[11] proposed a simple algorithm for procedure targeted spinal anesthesia and suggested 1% 2-chlorprocaine in a dose of 40 to 50 mg for ambulatory procedures requiring <T10 block and lasting less than 40 min. Although 35 mg dose has not been investigated in the past, the results of our study illustrate that it may also provide equally effective anesthesia with additional advantage of faster recovery.

Lower doses that do not provide effective anesthesia may not allow early discharge. Casati *et al.*[10] reported that although 30 mg provided faster block regression and shorter time to ambulate, no advantage was obtained in terms of voiding and home discharge. The reason may have been insufficient duration of anesthesia and significantly higher fentanyl requirement required in approximately 50% patients in the 30 mg group. The factors such as pain and higher fentanyl requirement are known to delay the voiding in the postoperative period.[14] As 35 mg dose provided effective anesthesia in our study, it may have improved the patient's willingness to ambulate and void after the regression of the block.

Voiding may not be considered essential discharge criteria after day care procedure. But we used more restrictive modified PADSS in our study as both gynecological procedures[15] and spinal anesthesia[16] predispose to postoperative urinary retention. Similar to the previous studies, the time required for voiding was the last criteria to be fulfilled in our study and was same as discharge time.[6,8,10] The hemodynamic parameters were well maintained throughout the procedure in most of the patients. Herndon *et al.*[5] reported lower incidence of intraoperative hypotension with the use of chloroprocaine as compared with bupivacaine (59.5% vs 83.8%) in total hip arthroplasty patients. As documented in the past studies, we did not record any significant adverse effects such as TNSs during the follow-up.[17,18]

Our study has several limitations. First, most of the procedures lasted less than 40 min despite 60 min being our inclusion criteria. Casati *et al.*[10] documented that fentanyl supplementation was required only after 30 min and was associated with the regression of the block. Hence, we would recommend this dose only for short procedures such as hysteroscopy, endometrial biopsy, dilatation, curettage, etc., Second possible flaw of our study was that we followed-up our patients only once, that is, after 24 h. However, these patients are routinely followed-up after 7 days in the surgical OPD and any anesthesia-related postoperative complication is always communicated for further evaluation. Third, limitation of our study was that our estimated sample size was small, that is, only 15 patients per group. A posthoc analysis would have helped in determining whether our study was adequately powered. An additional criticism of our study design could be the use of 5 mg dose difference which lead to similar results in two groups for certain variables. But the small dose difference used in our study helped us identify the lowest effective dose.

Conclusion

From our present investigation, we conclude that 35 mg 1% 2-chlorprocaine is superior to 40 and 45 mg doses as it not only provides effective anesthesia but also facilitates faster fulfillment of discharge criteria after short gynecological procedures. The stable hemodynamics and lack of incidence

of TNS are two additional benefits associated with the use of this local anesthetic in the ambulatory setting.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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