Indian Journal of Clinical Anaesthesia 2020;7(4):619–624

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Indian Journal of Clinical Anaesthesia

Journal homepage: www.ijca.in

Original Research Article

Comparing anaesthetic effects of intrathecal 2- Chloroprocaine with or without fentanyl in ambulatory surgeries- A prospective and randomized control study

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ARTICLE INFO

Article history:
Received 22-07-2019
Accepted 26-06-2020
Available online 25-11-2020

Keywords:
Ambulatory surgery
2-Chloroprocaine
Fentanyl
Spinal anaesthesia

ABSTRACT

Background: 1% 2-Chloroprocaine could have been an ideal local anaesthetic for ambulatory procedures but it has been neglected in past years and even after re introduction with its preservative and antioxidant free form.
Aim: To compare the anaesthetic effect of intrathecal 2-Chloroprocaine with or without fentanyl in patients undergoing short duration lower abdominal and lower limb surgeries regarding hemodynamic parameters, mean duration of block, time to ambulation and side effects.
Setting: Anesthesia Department at Narayana Multispeciality Hospital, Jaipur.
Design: Randomised, Comparative, Single Centre Study
Materials and Methods: A total of 120 patients,18-70 years, weight>50 kg and ASA grade I- II underwent elective lower abdominal and lower limb surgeries with expected duration <60 minutes were randomly allocated in two groups of 60 each to receive either 40mg 2- Chloroprocaine with saline or 25 μg fentanyl.
Statistical Analysis: Chi-Square and Unpaired Student T- Test ($p<0.05$).
Results: Spinal anesthesia was successful for all patients. Onset time of sensory and motor block, time to achieve peak block height and complete motor block was statistically insignificant ($p<0.05$). Time to complete sensory recovery was 105.87mins in fentanyl group and 69.17mins in saline group and time to compete motor recovery 80.13 mins in fentanyl group and 64.80 mins in saline group ($p<0.001$). Transient neurological symptoms were not found.
Conclusion: 2-Chloroprocaine spinal anesthesia provides rapid onset, giving it a promising profile for ambulatory surgery. Addition of fentanyl lengthens regression to S2 and with minimal increase of motor block duration.

1. Introduction

Short duration lower abdominal and lower limb surgeries are being done increasingly on ambulatory basis. An ideal anaesthetic for spinal anaesthesia in ambulatory surgeries would offer rapid onset of action, adequate potency, anticipated duration, and low incidence of side effects.

2-Chloroprocaine can be a better choice for ambulatory procedures.[1] 2-Chloroprocaine [benzoic acid, 4-amino-2-chloro-2-(diethylamino) ethyl ester, monohydrochloride] is an amino ester type of local anesthetic that was introduced by Foldes and Mc Nall in 1952.[2]

In the early 1980s, concerns about its use were raised following the description of nine cases of neurotoxicity after injecting large volumes of epidural 2-chloroprocaine.[3–5] Four out of nine patients were known to have unintentional intrathecal injections. The formulations of 2-chloroprocaine used at that time (Nescaine- CE) contained 0.2% sodium bisulfite as an antioxidant. In the literature, multiple studies have suggested that a combination of a low pH (<3) and presence of sodium bisulfite in the

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https://doi.org/10.18231/j.ijca.2020.112

anesthetic preparations, were the main culprits for the neurotoxicity observed.[6–9] Subsequently 2-Chloroprocaine was reintroduced for spinal anaesthesia in a preservative free and antioxidant free form and the pH of the solution was improved. This new formulation has been used at doses ranging from 30 to 60mg, which provides a spinal block profile similar to that of lidocaine in healthy volunteers and surgical patients and have not reported any case of neurological toxicity.[10–16]

The addition of intrathecal fentanyl has been used to prolong sensory blockage without delaying motor recovery.[17,18]

Thus, aim of our study was to compare the anaesthetic effect of intrathecal 2-Chloroprocaine with or without fentanyl in patients undergoing short duration lower abdominal and lower limb surgeries in ambulatory settings in terms of mean duration of block, hemodynamic parameters, time to ambulation, time to first analgesic dose and side effects.

2. Materials and Methods

After obtaining the approval by ethical committee of hospital and informed consent, 120 patients, aged 18 to 70 years, body weight >50 kg and ASA physical status I-II patients, undergoing elective lower abdominal and lower limb surgeries with expected duration of <60 mins in Anaesthesia Department at Narayana Multispeciality Hospital, Jaipur, Rajasthan were studied prospectively. Patients with ASA grade -III and IV, known allergy or sensitivity to study group drugs, failed blocks (if complete sensory and motor block not achieved in 20 minutes), known pseudo choline esterase deficiency or atypical pseudo choline esterase disease and other contraindications of subarachnoid block were excluded.

Before the scheduled surgery, pre-anaesthetic evaluation was done and Numeric Rating Scale for pain score on 0-10 were explained to the patient. In the operating room pre-operative vitals were recorded. Patients were divided into two groups (group C & F) and randomization was done by computer generated random number table. Under all aseptic condition, sub-arachnoid block was performed at the L3-L4 space via midline approach using 27G quincke's spinal needle. Patients in Group C received intrathecal inj. 1% 2-Chloroprocaine 4ml with 0.5ml normal saline and Group F received inj. 1% 2-Chloroprocaine 4ml with inj. Fentanyl 25 μg- 0.5ml. Patients were immediately laid supine for the remaining duration of the study as per protocol.

After spinal injection, a blinded assessor recorded the evolution of spinal block until achievement of complete recovery of block. Heart rate, mean blood pressure, respiratory rate, oxygen saturation and Modified Wilson sedation score were recorded at different time intervals till the complete recovery of block.

Sensory block was assessed using loss of pinprick sensation (blunt needle) in caudal to cephalad direction. The right $C_5 - C_6$ dermatome used as unblocked reference point. Time to onset (in minutes) was taken as time to onset of sensory block at S2 dermatome, Time to achieve peak block height was taken as the duration of time in minutes to achieve maximum dermatomal level of sensory block, Time to complete sensory recovery was taken as the duration of time (in minutes) from the onset time of sensory block till the time of recovery of S2 dermatome.

Motor block was assessed using a 4-point Modified Bromage score. Onset time in minutes (modified bromage grade =I), time to achieve complete motor block in minutes (grade =III) and time to complete recovery motor in minutes (grade =0). Time to ambulation (in minutes) was taken as when the patient was ambulated after complete recovery of block. Time to 1st post- operative analgesic dose (in minutes) was also noted which was given on the basis of Numeric rating scale for pain score $\geq$3.

Side effects observed were nausea, vomiting, hypotension (decrease in systolic arterial blood pressure $\geq$30% of baseline), bradycardia (defined as a decrease in heart rate below 45 beats per minute), respiratory depression, pruritus and local anesthetics toxicity. Patients were followed up for symptoms of headache, backache and TNS (Transient Neurological Symptoms).

2.1. Statistics

Sample size is calculated at 95% confidence level and alpha error 0.05 assuming expected standard deviation of 9 minutes in the time of ambulation within the two group as per reference article (spinal 2- Chloroprocaine: the added effect of fentanyl) to detect at least a difference of 5 minutes in the time of ambulation between the two groups. At study power of 80% required sample size of 52 cases in each group and considering 10% of the dropout a total of 60 cases were enrolled in each group.

Descriptive and Inferential statistical analysis was carried out in the present study using computer software (SPSS Trial version 23 and primer). Chi square test and unpaired student T Test was used at confidence level of 95% ($p< 0.05$).

3. Results

No statistically significant differences in age, gender distribution, ASA (American Society of Anesthesiologists) physical status and anthropometric variables were noted between the two groups (Table 1). The mean heart rate, mean blood pressure showed a gradual reduction during first 20-30 minutes in both the groups under the effect of neuraxial block and difference was statistically insignificant (P value > 0.05). No statistically significant difference was observed in respiratory rate, oxygen saturation and sedation

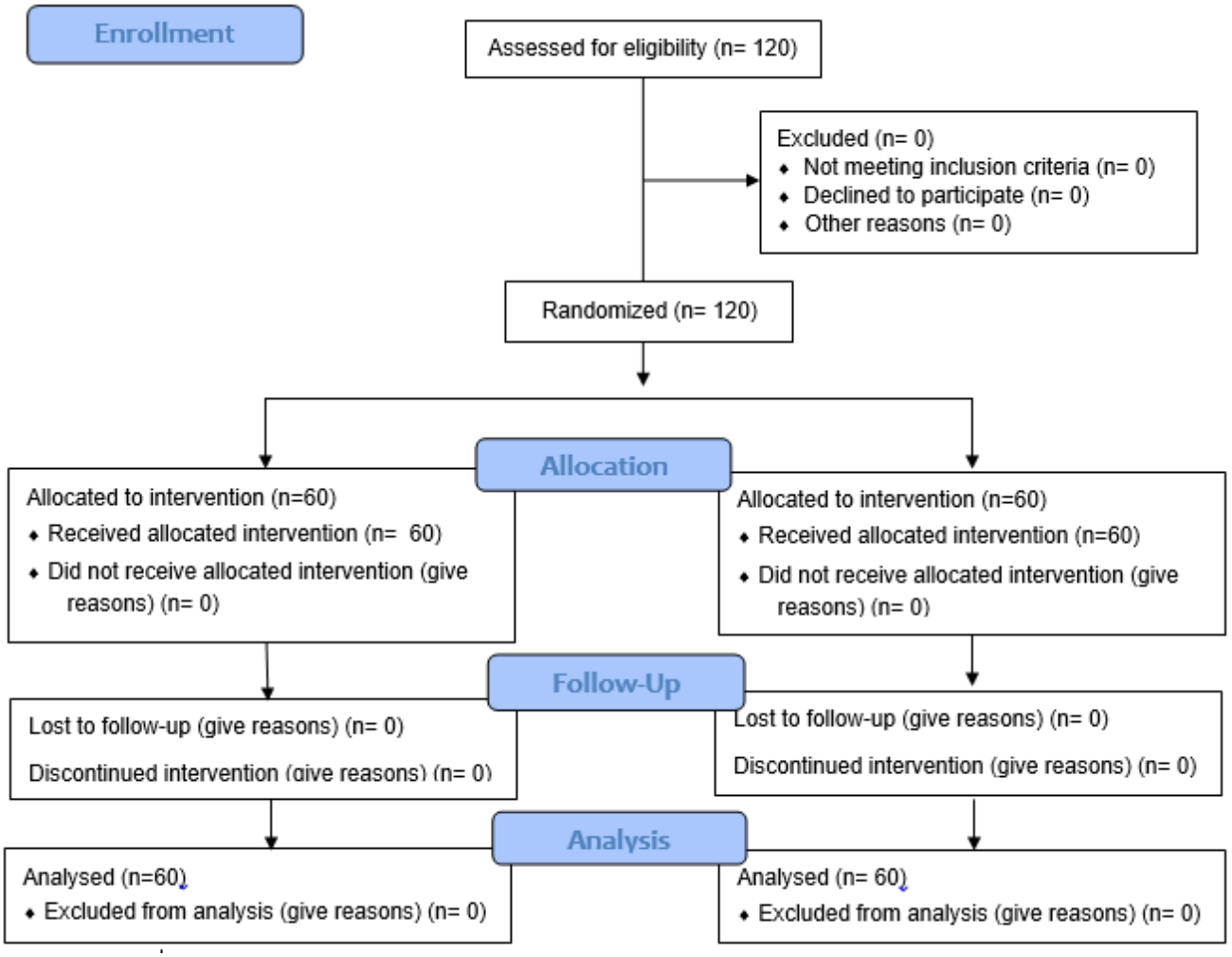

Diagram 1: Consort 2010 flow diagram

score among the groups.

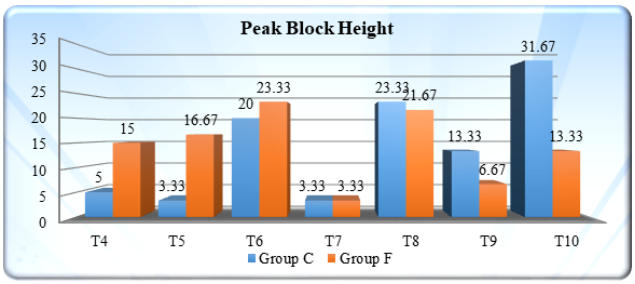

Fig. 1: Comparison of distribution of the cases according to sensory block- peak block height

Spinal anaesthesia was successful for all patients. Peak Block Height was higher in Chloroprocaine with fentanyl group (Figure 1) but it was statistically insignificant (P value = 1.000).

No significant difference was observed among both groups in onset time (p= 0.232NS) and time to achieve peak block height (p= 0.926NS) in sensory block and onset time (p=0.82NS) and time to achieve complete block in motor block (p=0.645 NS) (Table 1).

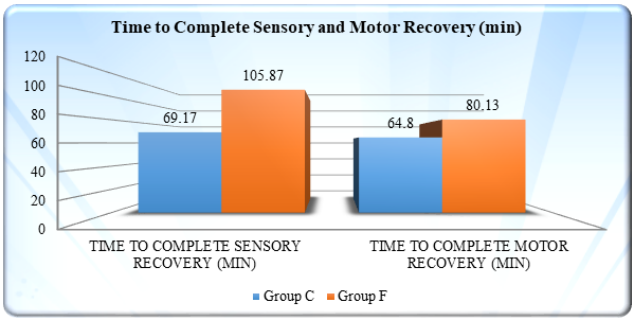

Fig. 2: Comparison of sensory and motor block variables

Table 1: Comparison of distribution of demographic data and outcome variables among the groups

Demographic Data	Group C(2-CP with Saline)	Group F(2- CP with Fentanyl)	P Value Level of Significance
Age (years- mean ± SD)	46.28±15.35	44.22±16.32	0.46 NS
Gender (No.- Male/Female)	20/40	21/39	1.000 NS
Weight (Kg- mean ± SD)	70.80±9.070	71.85± 9.704	0.542 NS
Height (cm-mean ± SD)	160.13±8.711	159.35±6.000	0.567 NS
BMI (Kg/m^2- mean ± SD)	27.72±3.90	28.31±3.63	0.39 NS
ASA physical status (No.- I/II)	30/30	40/20	0.096 NS
Outcome	Mean ±Std. Deviation	Mean ± Std. Deviation	P value-level of significance
Sensory block (in minutes)			
Onset Time	2.22±1.059	2.47±1.214	0.232 NS
Time to achieve peak block height	6.68±1.953	6.72±1.992	0.926 NS
Time **to complete sensory recovery**	69.17 ± 4.435	105.87 ± 13.398	<0.001S
Motor Block Duration (in minutes)			
Onset Time	3.73±1.635	3.80±1.505	0.82 NS
Time to Achieve Complete Motor Block	8.28±1.941	8.12±2.009	0.645 NS
Time to Complete Motor Recovery	64.80 ± 5.138	80.13 ± 10.009	<0.001S
Time To Ambulation	69.17±4.435	105.87±13.398	<0.001S
Time To 1st analgesic dose	59.97 ± 7.576	96.02 ± 13.515	<0.001S

The mean duration of sensory block as Time to complete sensory recovery was stastically significant longer in Chloroprocaine with Fentanyl group (105.87 ± 13.398 minutes) as compared to Chloroprocaine with Normal Saline group (69.17 ± 4.435 minutes) (Table 1 & Figure 2) (P value<0.001).

The mean duration of motor block as Time to complete motor recovery was stastically significant longer in Chloroprocaine with Fentanyl group (80.13 ± 10.009 min) as compared to Chloroprocaine with Normal Saline group (64.80 ± 5.138 min) and was significant (Table 1 & Figure 2) (P value<0.001).

Among the side effects it was observed that both the groups had episodes of hypotension (p=0.714 NS) and bradycardia (p= 1.0) which were statistically not significant, but pruritus was significantly seen in Fentanyl group (p= 0.036) (Table 2).

4. Disscussion

Spinal anaesthesia with 2- Chloroprocaine in comparison with general anaesthesia leads to significantly earlier discharge makes it a safe and favourable choice over general anaesthesia (Gebhardt V et al[19] 2018, Camponovo C et al 2014).[20]

2-Chloroprocaine is a short acting drug, thus allows rapid recovery of sensory/motor function, and effective alternative to Lidocaine for ambulatory surgeries without transient neurological symptoms. Similar results were found in the study by Breebaart MB et al[21] (2014), Goldblum E et al[6](2013), Vaghadia H et al[22] (2012), Hejtmanek MR et al.[23](2011), Casati A et al[15] (2007), Kouri ME et al[10] (2004). When 2- Chloropocaine was compared to Bupivacaine same results were found as discharge time, duration of block and time to ambulation was shorter with 2- Chloroprocaine (Lacasse MA et al.[24] - 2011), Teunkens A et al[25] - 2016).

All the demographic characteristics and ASA grading were comparable in both the groups (p >0.05).

The primary finding of this study is that the addition of 25 μg of intrathecal fentanyl to 2-Chloroprocaine spinal anaesthesia prolongs sensory blockade but only minimally lengthens motor blockade.

In our study peak block height was higher in Fentanyl group in comparison with Chloroprocaine with Normal Saline but it was statistically insignificant (p=1.000). These findings were consistent with the study by Vath JS et al[26](2004) and Chaudhary A et al[27](2014) which showed increase in peak block height when Fentanyl was used with Chloroprocaine and Ropivacaine respectively.

Adding of Fentanyl to local anaesthetic did not increase onset time of sensory/motor block, time to achieve peak block height in sensory block, time to achieve complete motor block in our study. (P value > 0.05)**.** Our results were consistent with Vath JS et al[26] (2004). Singh H et al[28] (1995), Chaudhary A et al[27] (2014).

The supplementation of intrathecal Fentanyl as an adjuvant to Chloroprocaine in appropriate dose produce good level of sensory block in all patients and addition of Fentanyl to Chloroprocaine prolongs duration of sensory block with less alteration in motor block. The similar results

Table 2: Comparison of side effects observed among the two groups

Side Effects Observed	Group C		Group F		Grand Total		P Value LS
	No	%	No	%	No	%	
Hypotension	3	5.00	5	8.33	8	6.67	0.714 NS
Bradycardia	3	5.00	4	6.67	7	5.83	1.0 NS
Nausea and Vomiting	0	0.00	0	0.00	0	0.00	NA
Pruritus	0	0.00	6	10.00	6	5.00	0.036S
Respiratory Depression	0	0.00	0	0.00	0	0.00	NA
Headache, Backache and TNS	0	0.00	0	0.00	0	0.00	NA

were found when addition of fentanyl to Chloroprocaine (Vath JS et al[26]-2004), bupivacaine (Singh H et al[28] -1995) and Kuusniemi KS et al[29] 2000) and lidocaine (Liu S et al[17] -1995) was done.

Time to Ambulation was delayed in Group F as compared with Group C which was stastically significant (P<0.001). The result of our study was consistent with Vath JS et al[26](2004).

In our study Time to first Analgesic Dose was significantly delayed in Chloroprocaine with Fentanyl group (P<0.001). Similar results was found in Singh H et al[28] (1995) who found intrathecal fentanyl reduced the analgesic requirement in the early postoperative period following Bupivacaine spinal block.

Limitation of our study was that we have compared only single dose of fentanyl with Chloroprocaine by which we can decide that addition of fentanyl is better for post-operative analgesia, but we cannot find out optimum dose of fentanyl for post- operative analgesia.

5. Conclusion

In our study, we found that spinal anaesthesia with 2-Chloroprocaine provides faster onset, predictable duration in terms of recovery of sensory and motor block as well as adequate potency for use in ambulatory procedures lasting for less than 60 minutes. Our study suggests that supplementation of intrathecal fentanyl as an adjuvant to Chloroprocaine in appropriate dose is an appealing choice for spinal anaesthesia for short duration surgeries in the ambulatory settings without affecting hemodynamic and respiratory parameters.

6. Source of Funding

None.

7. Conflict of Interest

None.

8. Acknowledgement

We want to thank Dr. Vinay K Gupta, Dr. Vishnu K Gupta (Acedemic and Research Department) and Opertion Theatre Team for their unconditional valuable support.

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Cite this article: Nagar A, Khandelwal R, Goyal PK, Pareek S, Bharti DK. Comparing anaesthetic effects of intrathecal 2- Chloroprocaine with or without fentanyl in ambulatory surgeries- A prospective and randomized control study. *Indian J Clin Anaesth* 2020;7(4):619-624.