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ORIGINAL RESEARCH

COMPARISON OF FENTANYL AND CLONIDINE AS ADJUVANTS TO INTRATHECAL 1% CHLOROPROCAINE IN INFRA-UMBILICAL SURGERIES

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ABSTRACT

Introduction: Spinal anaesthesia is a safe, reliable, inexpensive anaesthetic technique for regional anaesthesia. It also allows early ambulation and early rates of hospital discharges.

Material and methods: Present study was carried at tertiary care Hospital. After receiving ethical approval from the college ethical committee and CTRI registration, 64 patients aged 19 to 65 years old with ASA grade I and II physical status who were undergoing elective infra-umbilical surgeries were included in the study. Patients were randomly allocated in two groups of 32 patients each. Group C: Received 1% Isobaric Chloroprocaine 3 ml (30mg) + clonidine (30 mcg). Group F: Received 1% chloroprocaine 3ml (30 mg) + fentanyl (25 mcg). Total volume = 3.5ml. Sensory block was examined using pin prick method. Quality of motor block was examined and graded using Modified Bromage Scoring. Hemodynamic was monitored and side effects were noted.

Result: Total 64 patients were divided into two groups of 32 each. There were 17 males and 15 females in Group F. While in Group C, male and female participants were 16 each. In group F, mean onset time of sensory blockade was (3.69 ± 0.41min) and mean onset of motor blockade was (5.14 ± 0.65min). In group C, mean onset time of sensory blockade was (3.86 ± 0.28min) and mean onset of motor blockade was (5.31 ± 0.63min). In group F, mean duration of sensory blockade was (74.19 ± 3.14min) and mean duration of motor blockade was (60.24 ± 2.97min). In group C, mean duration of sensory blockade was (110.34 ± 8.45min) and mean duration of motor blockade was (94.88 ± 4.39min). In group F, 1 patient had hypotension and bradycardia while in

group C,4 patients had hypotension and 3 had bradycardia. Transient neurological symptoms, respiratory depression and pruritis were not seen in any of the groups.

Conclusion: From our study we conclude that, clonidine as an adjuvant to intrathecal chloroprocaine can be used for infra-umbilical ambulatory surgeries with good sub-arachnoid block quality and lesser side effects.

Keywords: Chloroprocaine, Clonidine, Fentanyl, Spinal anaesthesia, Ambulatory surgeries

INTRODUCTION

Spinal anaesthesia provides excellent operating conditions for surgery below the umbilicus. Shorter procedures, day care, and ambulatory surgery have been limited by the lack of an appropriate spinal local anaesthetic and the availability of fast-acting medicines.[1]

Spinal anaesthesia is a safe, reliable, inexpensive and the most common anaesthetic technique for regional anaesthesia used in surgical setting. It is easier to administer and hasvery fast onset of action, predictable duration, lower risk of infection, low failure rates, allows early ambulation and early rates of hospital discharges. Various local anaesthetics like Bupivacaine, Lignocaine, Chloroprocaine have been used intrathecally with or without adjuvants like opioids and alpha-adrenergic agonists.

Longer acting local anaesthetics can cause urine retention, pain after block regression, delayed ambulation, temporary neurological symptoms, and hypotension, among other things. Shorter procedures, day care, and ambulatory surgery have been limited by the lack of an appropriate spinal local anaesthetic and the availability of fast-acting medicines. [2,3]

The duration of surgery is dependent on a faster recovery from anaesthesia since the prolonged effect requires more constant monitoring in the post-operative ward, which disrupts hemodynamic stability and causes delayed micturition, ambulation, and finally discharge. Adjuvants help to reduce the dose of local anaesthetics, hence reducing adverse effects. [4,5]

To our best knowledge, there is no study comparing clonidine and fentanyl as adjuvants when applied intrathecally with chloroprocaine in our literature search. To close the gap, we undertook a randomized, double-blind research in healthy patients to assess intrathecal Fentanyl and Clonidine as adjuvants to Chloroprocaine. According to several previous studies, the dose chosen for this research work is the smallest effective dose with the fewer/no side effects.

MATERIAL AND METHODS

Present study was carried at tertiary care Hospital. After receiving ethical approval from the college ethical committee and registration with **Clinical Trial Registry of India (CTRI/2021/02/031470)**, 64 patients aged 19 to 65 years old with ASA grade I and II physical status who were undergoing elective infra-umbilical surgeries were included in the study(Table 1). Each patient was randomly allocated to one of the two groups of 32 patients each. **Group C**: patients were scheduled to receive 1% Isobaric Chloroprocaine 3 ml (30mg) + clonidine (30 mcg), i.e. 0.2 ml after dilution with 0.3ml of 0.9% normal saline. **Group F**: patients were scheduled to receive 1% chloroprocaine 3ml (30 mg) + fentanyl (25 mcg), i.e. 0.5 ml(Table 1). Total volume = 3.5ml.

All the patients received complete pre-anaesthetic evaluation on the day previous to surgery. Thorough general and systemic examination was done including airway and the surface anatomy where sub-arachnoid block was to be delivered. After informed and written consent, the procedure to be carried out was explained and the patients were reassured to alleviate their anxieties. All the patients were kept nil per oral 6 hours prior to surgery. All of them received Tab. Alprazolam 0.25 mg and Tab. Ranitidine 150 mg at night before the surgery. Intravenous (i.v) line was secured on the day of surgery, and i.v fluid Ringer Lactate was begun at a rate of 15ml/kg 30 minutes before surgery, and maintenance fluid was given as per Holiday Segar[1] formula. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, arterial oxygen saturation, and electrocardiogram (ECG) were recorded after premedicating with injection (Inj.)Ranitidine 50mg i.v, and injection (Inj.)Ondansetron 4mg i.v.

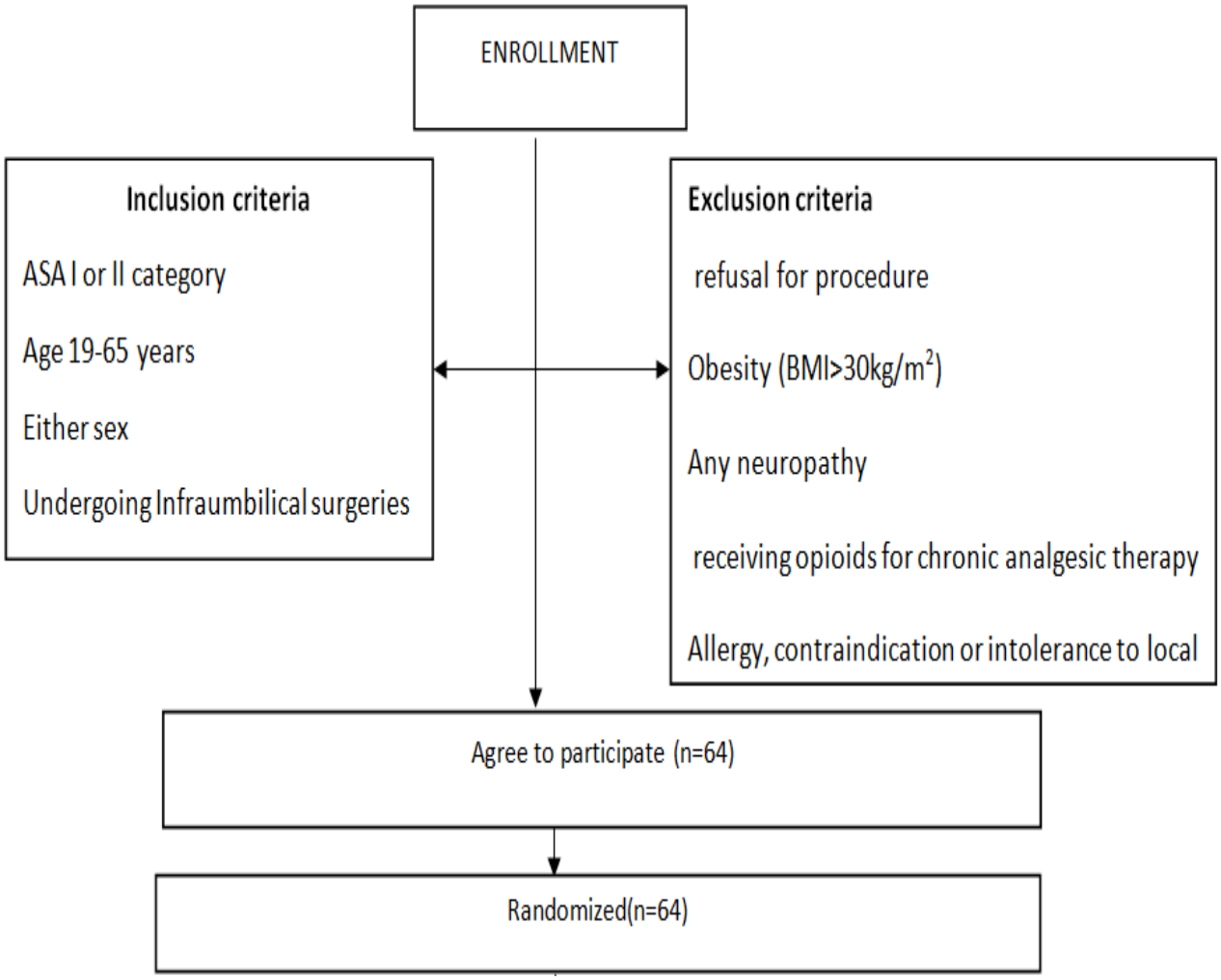
Patients were given spinal anaesthesia in the L2-L3 intrathecal space while seated, utilizing a midline technique with a 25G spinal (Quincke's needle. Patients received a preservative-free formulation of isobaric 1 percent chloroprocaine 30 mg, along with fentanyl or clonidine, according to their trial group. Patients were made supine soon after spinal anaesthesia. Following spinal anaesthesia, the patients were given Inj. Midazolam 1mg iv. The patient's heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and arterial oxygen saturation were monitored.

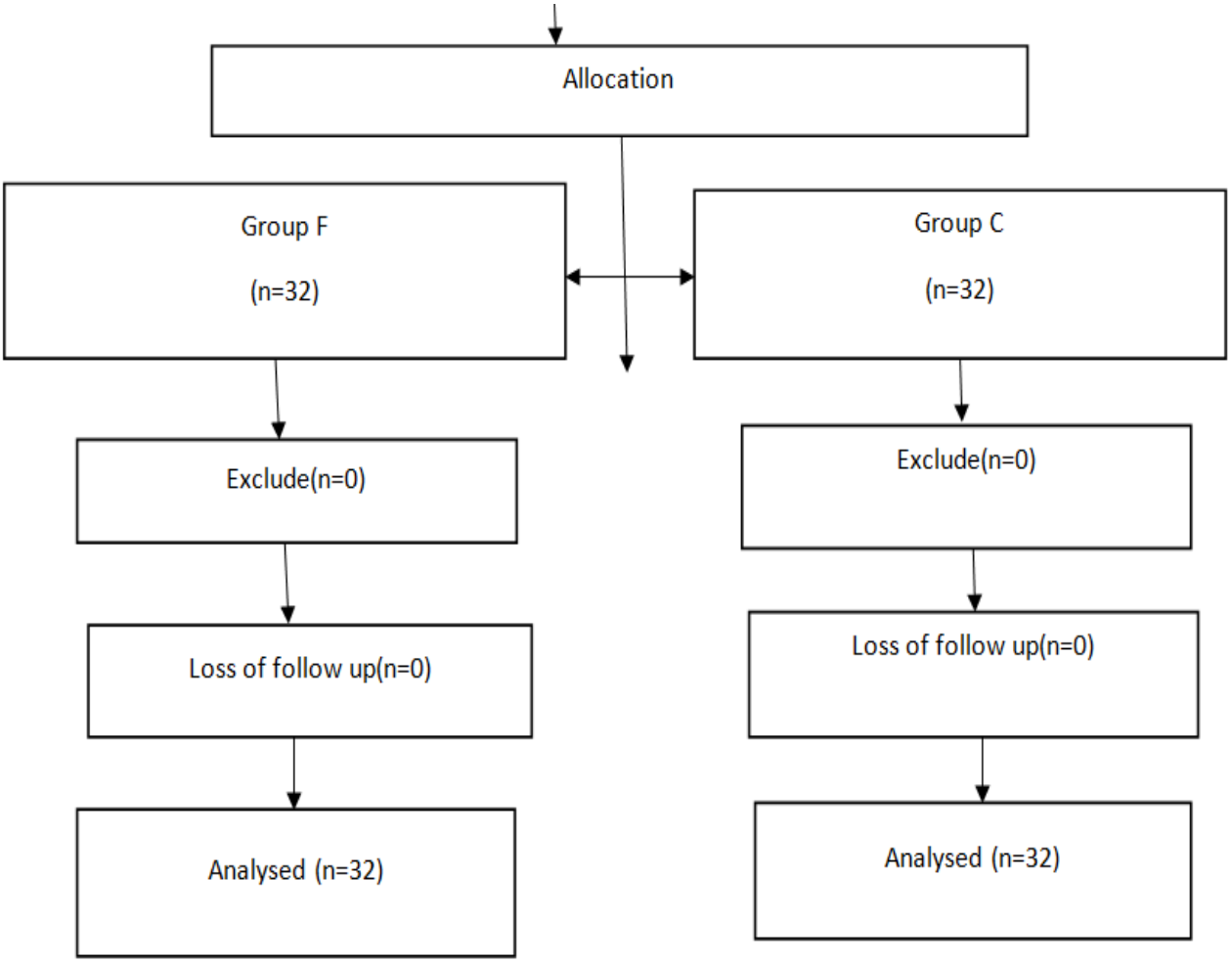
The sensory level of the block was measured from the caudal to the cephalad. The loss of feeling to pin prick was utilized to determine sensory block, with the C5-C6 dermatome serving as an unblocked reference point. The Modified Bromage Scale was used to evaluate the motor block. [1]The disappearance of pin prick sensation $\geq$ T10 with modified Bromage 2[1] defines readiness for operation. If the patient complained of pain, the research was stopped and Inj. Butorphanol1mg iv was given. If the patient continued to experience discomfort, general anaesthesia was administered to continue the case; nevertheless, the patient was not included in this study. Any complications, side effects, or undesirable impacts were recorded.

OBSERVATIONS/RESULT

Total 64 patients were enrolled in this study divided into two groups of 32 each(Table 1).

Table 1: Consort diagram of study enrollment


ENROLLMENT
Inclusion criteria
ASA I or II category
Age 19-65 years
Either sex
Undergoing Infraumbilical surgeries
Exclusion criteria
refusal for procedure
Obesity (BMI>30kg/m2)
Any neuropathy
receiving opioids for chronic analgesic therapy
Allergy, contraindication or intolerance to local
Agree to participate (n=64)
Randomized(n=64)



There were 17 males and 15 females in Group F (Table 2).

Table 2: Comparison of demographic data and block quality between two groups

Characteristics	Group F	Group C	p value
Male	17	16	>0.05
Female	15	16	>0.05
Age	37.91±13.96	39.84±13.29	>0.05
Weight	50.75±5.95	52.78±7.53	>0.05
Sensory onset	3.69±0.41	3.86±0.28	>0.05
Motor onset	5.14±0.65	5.31±0.63	>0.05
2 segment regression	59.72±5.18	85.53±7.91	<0.001
Sensory duration	74.19±3.14	110.34±8.45	<0.001
Motor duration	60.24±2.97	94.88±4.39	<0.001

While in Group C, male and female participants were 16 each. All patients were having weight in between 50-80 Kgs. In group F, mean onset time of sensory blockade was (3.69 ± 0.41 min) and mean onset of motor blockade was (5.14 ± 0.65 min)(Table 2). In group C, mean onset time of sensory blockade was (3.86 ± 0.28 min) and mean onset of motor

blockade was (5.31 ± 0.63 min)(Table 2).The maximum peak height achieved in both Group F and Group C was upto T6 level. Mean 2-segment regression in Group F was achieved earlier (59.72 ± 5.18); than that in Group C (85.53 ± 7.91), which was found to be statistically significant with a p-value of < 0.001 (Table 2). In group F, mean duration of sensory blockade was (74.19 ± 3.14 min) and mean duration of motor blockade was (60.24 ± 2.97 min)(Table 2). In group C, mean duration of sensory blockade was (110.34 ± 8.45 min) and mean duration of motor blockade was (94.88 ± 4.39 min)(Table 2). Out of 32 patients in Group F, 1 patient had hypotension managed by intravenous fluids, bradycardia noted in 1 patient for which intravenous Atropine 0.6mg was given, 3 patients complained of post operative nausea vomiting managed by intravenous ondansetron 4mg; while 4 patients complained of shivering in post operative period which recovered with due time(Figure 1,2,3,4).

Figure 1: Comparison of mean Heart Rate

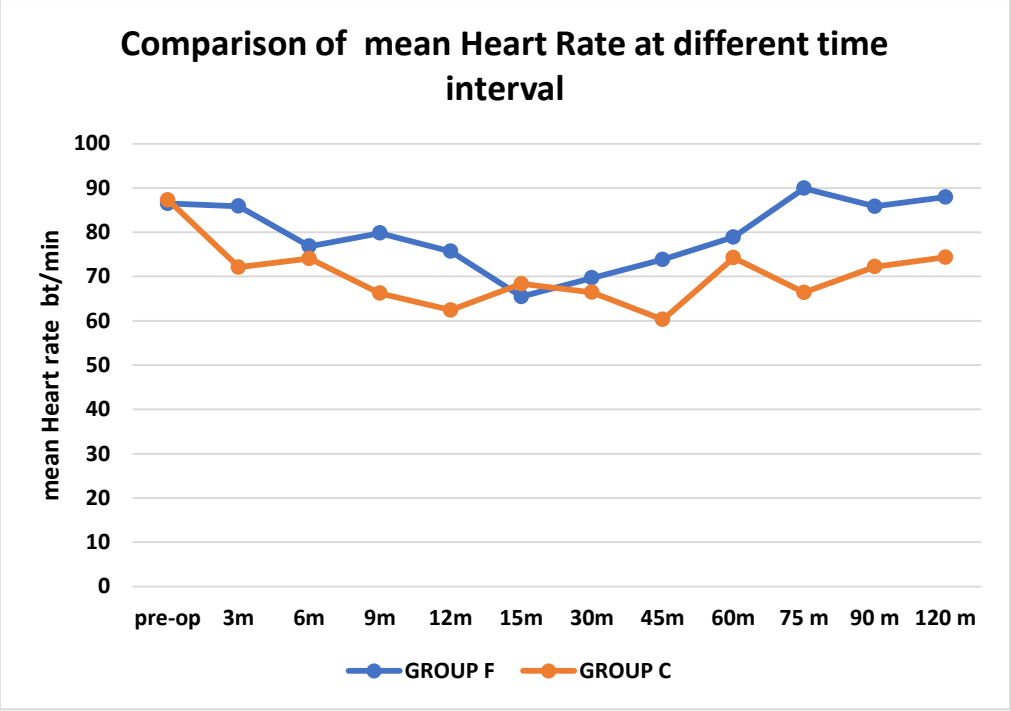


Figure 2: Comparison of mean SBP

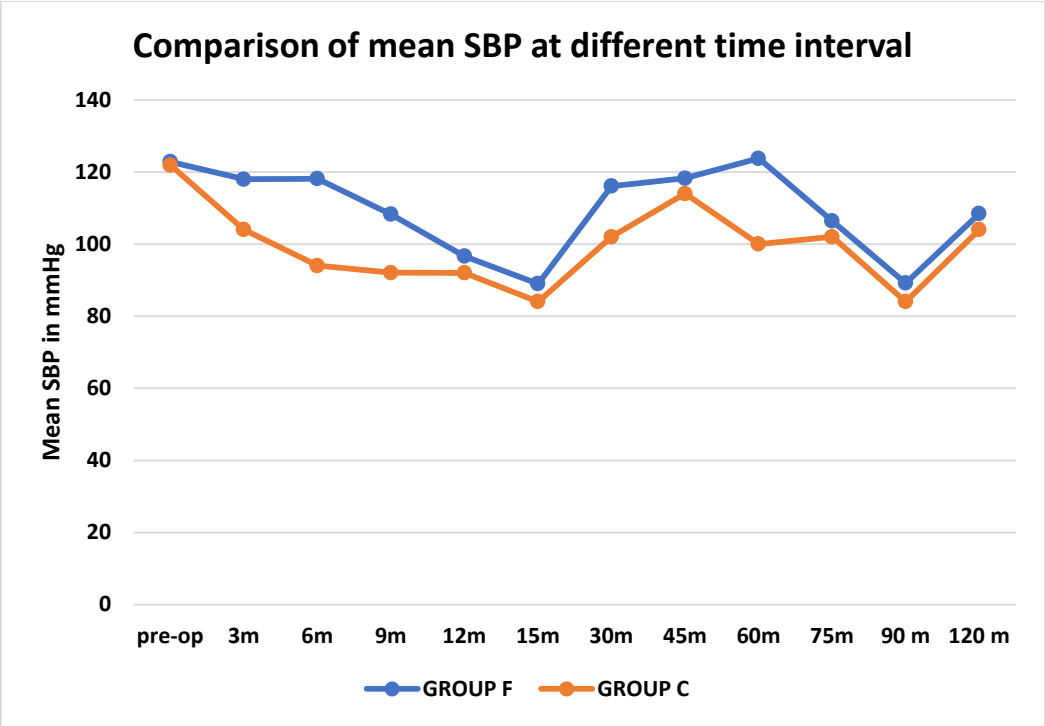


Figure 3: Comparison of mean DBP

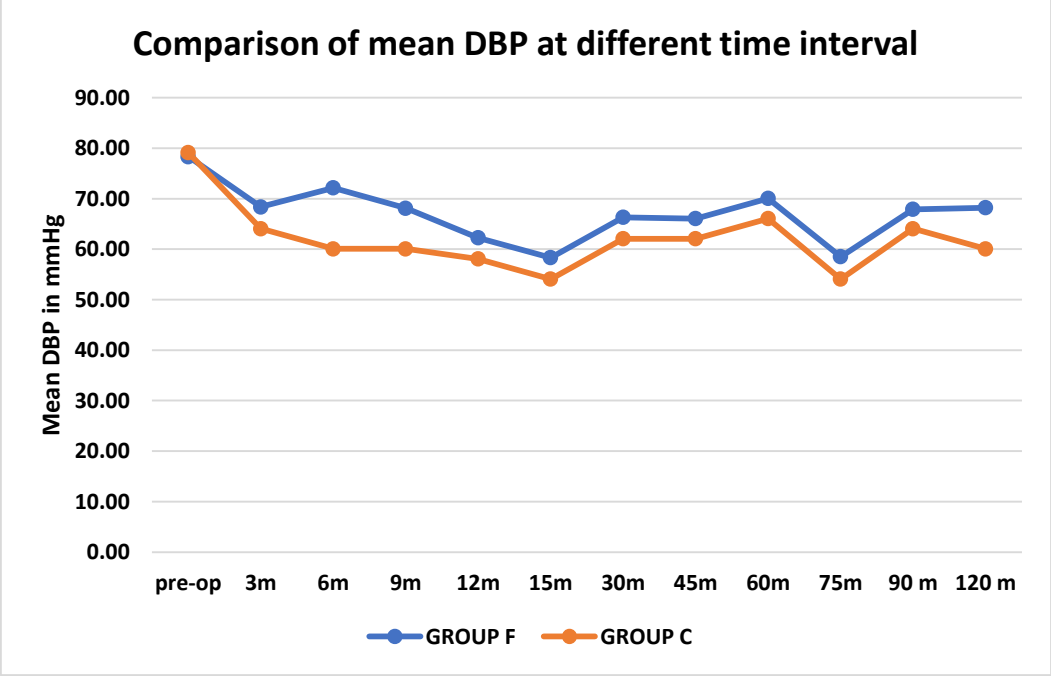
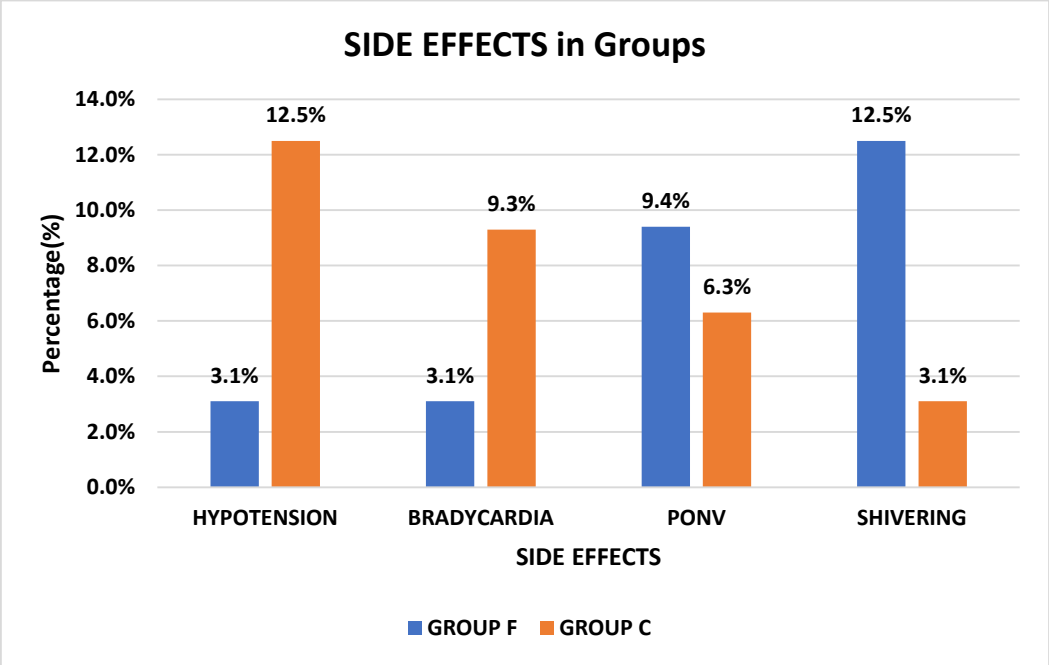


Figure 4: Side effects in Groups



While out of 32 patients in Group C, 4 patient had hypotension out of which 2 were managed by intravenous fluids and rest 2 required single shot of intravenous Mephentermine 6mg ; bradycardia noted in 3 patients out of which 2 patients received intravenous Atropine 0.6mg while 1 patient recovered spontaneously , 2 patients complained of post operative nausea vomiting managed by intravenous ondansetron 4mg while 1 patients complained of shivering in post operative period which recovered with due time (Figure 1,2,3,4).Transient neurological symptoms, respiratory depression and pruritis was not seen in any of the groups. Our observations on side effects were found to be statistically insignificant on comparison between both groups. Patients in Group F were found to be more hemodynamically stable in intra-operative and post-operative period than in Group C.

DISCUSSION

Intrathecal use of 2-chloroprocaine was described in 1952. The dose ranges from 20 to 60 mg, with 40 mg as a usual dose. We have taken 30 mg dose of chloroprocaine for our study. **Förster JG *et al*** [6]compared short-acting local anaesthetics articaine, chloroprocaine, and prilocaine for ambulatory spinal anaesthesia and finds Chloroprocaine an appealing option for spinal anaesthesia. **Casati *et al***[7]concluded that the Chloroprocaine 30 mg had insufficient duration of spinal blockade and suggested adding adjuvants. **Kopacz *et al***[3] concluded that the 10mg is a no effect dose, 20mg and 30mg produced adequate sensory anaesthesia but limited motor blockade with occasional sacral sparing. So, we decided to add adjuvants to chloroprocaine.In this research work, there was no statistically significant difference ($p>0.05$) in age among the groups showing comparability of the groups in respect of age. **Ganesh M *et al*** [8],**Chetty DK *et al*** [9],**Verma S *et al*** [10],**Sinha R *et al*** [11],**Singariya G *et al*** [12] also in their respective studies found that, there was no remarkable differentiation established between

two groups relating to demographic data similar to our study. In the present study the mean time of onset of sensory blockade in Group F was 3.69 ± 0.41; while in Group C was found to be 3.86 ± 0.28. The difference was statistically insignificant among the groups (p>0.05)(Table 2). **Davis BR *et al*** [4] conducted a study to compare the effect of adding 15 mcg Clonidine to 30mg Chloroprocaine and their results were similar to our study as they didn't find any significant change in duration of onset of sensory block. Another author **Verma S *et al*** [10]also found results similar to that of our study as in addition of clonidine to chloroprocaine had onset time of sensory blockade around 3 to 4 mins as in our study. **Arora R *et al*** [13], conducted study on 75 patients by using intrathecal bupivacaine with clonidine in doses of 15 mcg and 30 mcg and they found early onset of sensory blockade in group of patients who received clonidine with bupivacaine intrathecally, which is dissimilar to that of our study observations.

In our study, time for 2 segment regression was observed to be statistically earlier in group of patients who got spinal anaesthesia with Chloroprocaine along with Fentanyl. In the study done by **Agarwal *et al***[14] time to two segment sensory regression was statistically more in group of patients who received 30mcg Clonidine as an adjuvant to spinal block. Same results were found by **Dobrydnjov I *et al*** [15] who conducted a study on 45 patients who received intrathecal 6mg bupivacaine alone and with 15 mcg or 30 mcg clonidine and they found statistically significant enhancement of duration for two segment sensory regression by adding clonidine as an adjuvant to intrathecal bupivacaine. **Singariya G *et al***[12] in their study concluded that intrathecal preservative-free 1% 2-chloroprocaine (30 mg) with fentanyl (25 µg) as an adjuvant result in a faster onset, prolonged duration of sensory blockade, 2-segment regression time and postoperative analgesia, when compared to preservative-free 1% 2-chloroprocaine (30 mg) without an adjuvant, in patients undergoing elective lower segment caesarean section.

The mean duration of sensory blockade was statistically significant (p<0.001) and prolonged in the group who received Chloroprocaine with Clonidine intrathecally (Table 2). **Kanazi GE *et al*** [16] conducted study on intrathecally 12mg Bupivacaine with added effect of 3mcg Dexmedetomidine and 30 mcg Clonidine and they also found statistically significant augmentation of duration of sensory block with the use of Clonidine as an adjuvant. **Singh G *et al*** [17] conducted a study on intrathecal Bupivacaine with Fentanyl and Clonidine as adjuvant and found addition of adjuvants prolonged duration of block. In patients having anorectal operations, **Yadav *et al***[18] examined the efficacy of additional adjuvants i.e, fentanyl and clonidine to hyperbaric bupivacaine as spinal anaesthesia and concluded that adjuvants generated sustained intraoperative and postoperative analgesia along with faster onset and prolonged duration of spinal block; similar to that of our study observations.

In the present study the mean time of onset of Bromage 3 blockade was statistically insignificant among the groups (p>0.05)(Table 2).In a study done by **Singh G *et al*** [17]; they compared the effect of Clonidine used as an adjuvant to intrathecal Bupivacaine and they did not find any statistically significant difference in onset of motor blockade among the groups. In our study we found mean time of total duration of motor block prolonged in group of patients who received clonidine as an adjuvant to intrathecal chloroprocaine. **Bhaskara B *et al***[19] conducted a prospective randomized comparative study using intrathecal 1% chloroprocaine (3ml) with 12.5 mcg fentanyl versus 1.5ml of 0.5% ropivacaine with 12.5

mcg fentanyl intrathecally in day care perianal surgeries. He found that chloroprocaine provided adequate duration and depth of surgical anaesthesia for short procedures with advantages of faster block resolution and earlier hospital discharge when compared to spinal ropivacaine. Thus, making intrathecal chloroprocaine a good choice for elective infra-umbilical day care ambulatory surgeries.

In group F, one patient had hypotension and bradycardia while in group C, four patients had hypotension and three had bradycardia(Figure 1,2,3). Transient neurological symptoms, respiratory depression and pruritis was not seen in any of the groups. In the study done by **Kouri ME *et al*** [20]on Chloroprocaine has shown mild hemodynamic changes and none of patient needed vasoactive agents. Study done by **Dobrydnjov I *et al*** [15] on 45 patients with intrathecal 12 mg hyperbaric bupivacaine alone and with 15 mcg or with 30 mcg clonidine and they found that 5% patients experienced bradycardia out of which 1 patient was given 0.25 mg injection Atropine to treat bradycardia. Study done by **Siddaiah*et al*** [22], **Teunkens A *et al*** [23], **Lacasse MA *et al*** [24], on Chloroprocaine and they found incidence of bradycardia was 1%, 3%, 6% respectively. Study done by **Dobrydnjov I *et al*** [15] on hyperbaric bupivacaine alone and with clonidine shown post-operative nausea vomiting in 13.3% of patients and 3.3% patients had complain of pruritis.In 1980s, neurotoxicity was reported in 8 patients after accidently receiving large doses of intrathecal injection of bisulphite containing chloroprocaine[6].Although chloroprocaine in current use is preservative free.In our study there was no incidence of transient neurologic symptoms.**Casati *et al***[7] compared 30 mg, 40 mg, and 50 mg chloroprocaine doses in lower limb surgery and found no transient neurological symptoms. **Verma S *et al***[10] compared 30mg intrathecal chloroprocaine alone in one group with another group who were given 30mg chloroprocaine along with 30 mcg clonidine intrathecally in patients undergoing elective lower abdomen and lower limb surgeries and found no significant adverse effects in the patients while conducting the study, similar to our study.

CONCLUSION

After making all observations and analysing our data statistically and comparing them with previous studies, we conclude that, addition of clonidine or fentanyl does not affect time of onset of sensory or motor block. The duration of sensory and motor block as well as the time taken for 2-segment regression of sensory block is found to be more in the group of patients who received clonidine as an adjuvant to intrathecal chloroprocaine.Hemodynamically, addition of fentanyl to chloroprocaine gives better stability when compared with clonidine. The incidence of side effects like shivering, pruritis, PONV (post operative nausea vomiting) was lesser in patients who received clonidine as an adjuvant to chloroprocaine.

There is a **possible limitation in this study** that could be addressed in future research work; post operative analgesia needs to be studied and discussed separately as, we mainly studied the intraoperative part and the efficacy of these adjuvants with the local anaesthetic of choice.

Thus, we conclude that, clonidine as an adjuvant to intrathecal chloroprocaine can be used for infra-umbilical ambulatory surgeries with good sub-arachnoid block quality and lesser side effects.

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