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Comparative Effects of Fentanyl and Clonidine with Chloroprocaine, Respectively, in Lower Limb and Abdominal Surgery

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KEYWORDS

CL,
F,
CP,
NS,
anesthesia,
SA-B technique.

ABSTRACT:

Research findings have indicated that CP exhibits a more rapid recovery from anesthesia in comparison to 0.5% Bupivacaine. Furthermore, previous research has determined that the neuraxial administration of CL effectively suppresses the release of spinal substance P. Additionally, research findings have indicated that F exhibits a significantly lower affinity for kappa receptors situated in the spinal cord. Therefore, the objective of our study was to evaluate and compare the effects of CP in combination with F and CP in conjunction with CL.Sixty patients were split evenly. Both Group C and Group F were given CP in addition to CL and NS, respectively. In addition to this ,(T, PR, BP, RR,CNS, CVS, lungs, and airways, etc.), a full hemogram (including PT, BT, CT, BSL, CU, SE, X-ray of the chest in the PA view, and ECG) was performed. No medications were given to any patients prior to the start of the anesthetic procedure. All patients were briefed on the SA-B technique.In our study, we found that on comparing PR at STI, statistically significant variation was observed at 30min, 45min, 60min, 75min,75min& 90min, as the p values were 0.047, 0.018, 0.002, 0.001, and 0.011, respectively, and on comparing MAP at STI, significant variation was observed at 0min, 5min, and 10min, as the p value was 0.000.It has been observed that low-dose (1%) CP in conjunction with either F or CL as an adjuvant is beneficial in procedures with a duration of less than 90 minutes.

INTRODUCTION

According to past studies, Karl August Bier was the first to use spinal anesthesia in clinical practice in 1898.[1] Furthermore, various studies revealed that , both elective and emergency lower abdominal surgeries (LAS), including caesarean sections (C-section), orthopaedic, and urological procedures, it is still one of the most popular surgical techniques after more than a century.[2] Multiple studies have documented that clonidine functions as a centrally acting, selective partial agonist of the alpha-2 adrenergic receptor and imidazoline receptor. The activation of postganglionic alpha-2 receptors in the substantia gelatinosa of the spinal cord results in analgesia.[3] Studies have also shown that F primarily binds to mu receptors. The activation of mu receptors in the supraspinal region results in the production of analgesia. Additionally, it exhibits a weak interaction with kappa receptors that are situated in the spinal cord.[4,5] Studies have also shown that CP has a faster recovery from anesthesia compared to 0.5% Bupivacaine. As a result, the patient is able to ambulate more quickly after receiving CP.[4,5] There have been studies conducted to examine the impact of single adjuvants like F and CL when combined with CP. The comparison of the different combinations, however, has not been examined.[6,7] Hence, in our study, we have compared the effects of chloroprocaine (CP) in combination with fentanyl (F) and CP in conjunction with clonidine(CL).

AIM

To compare and evaluate the efficacy of F and CL as adjuvants to intrathecal 1% CP in lower limb(LL) and LAS lasting <90 minutes.

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INCLUSION CRITERIA

1. ASA physical status I and II
2. Short surgical procedure lasting <1hr 30min.
3. Both male & female were include

EXCLUSION CRITERIA

1. ASA III&IV status.
2. Patients who were Contraindicated to regional anesthesia
3. Significant coexisting systemic disorders like neuromuscular diseases, neuronal degenerative disorders, bleeding and hematological disorders, cardiac disorders, or gestational diabetes
4. Patients with spine deformity
5. H/o of allergy to bupivaccaine or clonidine.
6. H/o of opioid, clonidine medication or magnesium treatment prior to surgery.
7. Parturient
8. Patient refusal
9. H/o of seizure

MATERIAL & METHOD

We have conducted a prospective, randomized, double-blind, comparative study at KIMSH, Karad, on patients for elective LAB and LL surgery starting in 2017 and ending in 2019 after getting ethical approval and written informed consent from 60 included patients. Further, these 60 patients were randomly divided into 2 groups, i.e., group F and group C. Group F received 2.5 ml of 1% CP + F 0.5 ml and Group C received 2.5 ml of 1% CP + CL 0.2 ml and 0.3 ml of NS. Aditionally detailed history of underlying medical illness(MI), previous surgery(PS), anesthesia(A), and hospitalization(H) were taken. The general condition of the patient, vital signs, ht and wt, CVS, respiratory system, CNS, vertebral column(VC), airway assessment(AA), complete hemogram PT, BT, CT, BSL,creatinine urea(CU), serum electrolyte(SE), X-ray chest PA view, and ECG were checked. Patients were advised to be nil per orally according to ASA guidelines. Further, no drug were administered to any patients prior to the induction of anesthesia. The procedure of sub-arachnoid block(SA –B) was explained to all patients.

MATERIAL

In our study, we used the following equipment for our study procedure: a pre-sterilized tray that contained sponge-holding forceps, a gauze piece, a hole towel, a gown, povidine, iodine, chlorhexidine, a disposable spinal needle (25G or 23G), a 5ml disposable syringe, a pair of sterile gloves, an 18-gauge sterile needle for testing a pin prick, anesthesia work station, a laryngoscope, cuffed endotracheal tubes (sizes 6.5 to 8.5), suction apparatus, suction catheters 14 and 16 FG, a defibrillator, a sphygmomanometer, and ECG electrodes. Study drugs such as inj.CP1%, inj. CL150µg/ml, and inj. F 50µg/ml. Other drugs like inj.midazolam (1 mg/ml), NS, ringer lactate,emergency drugs like atropine, adrenaline, dopamine, dobutamine, isoprenaline, hydrocortisone, glycopyrolate, mephenteramine, ephedrine, phenylephrine, morphine, dexamethasone, sodium bicarbonate, calciuum-gluconate, xylocard, digoxin, nitroglycerine, deriphylline, avil, furosemide, ranitidine, metoclopramide, and phenytoin, an ECG monitor, pulse oximetery, and a non-invasive(NI) BP instrument were placed in our OT.

METHOD

In our study, we measured baseline pre-OP parameters before inducing anesthesia. 100% of oxygen with an oxygen mask at 4 L/min was started. IV line was secured with 20G or 18G iv canalua to start iv drip with ringer lactate(RL) or NS as per patient condition. The patient was put in a right or left lateral position with the help of an assistant. Under all aseptic precautions, lumbar SA-S was identified preferably at L3–4 intervertebral space using a 25-g disposable Quincke's spinal needle. Both groups received their respective drugs; hence, the total volume injected was 3 ml in both groups after achieving free flow of CSF. The punctured site was sealed with a sterile gauze piece and micropore after the block. The patient was turned in a supine position. NIBP, HR, O2 saturation, and level of sensory and motor block were monitored. Intra-operative monitoring includes NIBP, PR, continuous ECG, PO, and urine output (UO) if required. Assessment of sensory block was tested by pin pricking bilaterally in the midclavicular line with an 18G needle every 2 minutes.Post-Op HR, NIBP,SB,Visual Analog Scale (VAS), Bromage Score, and Sedation Score (SS) were recorded at every 165-minute interval for the first 2 hours and then every 1 hour for 24 hours. Rescue analgesic (inj. Tramadol 100mg IV or inj. Diclofenac IV) was administered at a VAS score >4, and time was noted. The time from intrathecal injection to the

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first request of analgesic (i.e., duration of analgesia) was noted. Total analgesic dose in the first 24 hours was recorded. The incidence of AEs such as nausea, vomiting, shivering, pruritus, RD, S, and hypotension was recorded.

Score	Criteria
0	No pain
1, 2, 3	Mild pain
4, 5, 6	Moderate pain
7, 8, 9	Severe pain
10	Worst imaginable pain

Table1: VAS

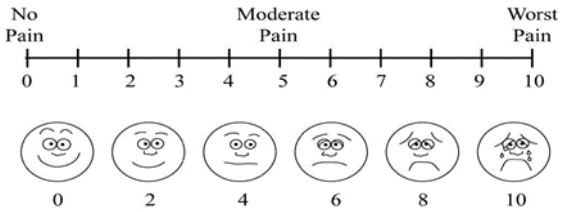

Figure1: VAS

SEDATION SCORE

1. Awake & alert
2. Sedated, responding to verbal stimulus
3. Sedated, responding to mild physical stimulus
4. Sedated, responding to moderate or severe physical stimulus
5. Not-arousable

STATISTICAL ANALYSIS

SPSS version 20.0 was used for stastical analysis.Comparison of continuous variables between groups was analyzed using student t test. Norminal categorical data between group was compared using fisher exact test .

RESULT

AGE GROUPS (years)	GROUP F	GROUP C
≤20	1 [3.33%]	1 [3.33%]
21-30	9 [30%]	7 [23.33%]
31-40	4 [13.33%]	2 [6.66%]
41-50	10 [33.33%]	13 [43.33%]
51-60	6 [20%]	7 [23.33%]
Mean ± SD	45.3 ± 19.93	49.7 ± 19.62

Table 2: Age wise distribution

In our study, we found that the mean age observed in group F was 45.3±19.93 and in group C was 49.7±19.62 (Table 2).

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Gender	GROUP F	GROUP C
Male	14 [47%]	19 [63.33%]
Female	16 [53%]	11 [36.67%]
TOTAL	30	30

Table 3: Gender-wise

In our study, we found that in group F, there were 14 males & 16 females, and in group C, there were 19 males &11 females (Table 3).

WEIGHT (kgs)	GROUP F	GROUP C
40-49	3 [10%]	6 [20%]
50-59	9 [30%]	4 [13.33%]
60-69	8 [26.66%]	8 [26.22%]
70-79	2 [6.66%]	7 [23.33%]
80-89	6 [20%]	4 [13.33%]
90-99	2 [6.66%]	1 [3.33%]
Mean ± SD	65.56 ± 15.03	65.1 ± 14.58

Table 4: Wt in both groups

In our study, we found that the mean wt observed in groups F & C was 65.56kg & 65.1kg, respectively (Table 4).

HEIGHT (cms)	GROUP F	GROUP C
140-149	-	1 [3.33%]
150-159	8 [26.66%]	10 [33.33%]
160-169	19 [63.33%]	17 [56.66%]
170-179	3 [10%]	2 [6.66%]
Mean ± SD	162.53 ± 5.2	162.06 ± 5.88

Table 5: Ht in both groups

In our study, we found that the mean ht observed in groups F & C was 162.53cm & 162.06 cm respectively (Table 5).

SURGERY	GROUP F	GROUP C
Dilatation and curettage	6	2
Cystoscopy	2	4
DJ stenting	6	4
Hysteroscopy	2	1
Optical urethrotomy	5	6
Lower limb wound debridement	3	5

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Resuturing of wound gape	2	4
Bartholin‟s cyst marsupalisation	4	-
Fistulectomy	-	1
TURP	-	1
STSG	-	2
TOTAL	30	30

Table 6: Surgeries in both group

In our study ,we found that both groups were comparable with respect to the type of surgery (Table 6).

	GROUP F	**GROUP C**
Mean±SD	8.54± 1.53	9.67± 3.99
p value	**0.000**	

Table 7: Duration of onset of sensory block (D-OSB)

In our study, we found that, by using an unpaired t-test, D-OSB between 2 groups was found to be statistically significant, as the p value was 0.000 at the mean difference (1.12 min). Thus, the OSB was faster in group F when compared to group C (Table 5).

	GROUP F	**GROUP C**
Mean ± SD	9.7 ± 2.6	6.71 ± 2.7
p value	0.82	

Table 8: D-OMB

In our study, we found that, by using unpaired t-test on comparing the D-OMS between 2 groups p value was 0.82 thus was found not statistically significant (Table 8).

	GROUP F	**GROUP C**
Mean ± SD	12.47 ± 3.14	15.32 ± 6.16
p value	0.199	

Table 9: Duration(D) required to achieve highest level of SB

In our study,we found that, using an unpaired t-test,on comparing D between 2 groups, the p value was 0.199, thus being found to be not statistically significant (Table 9).

SENSORY LEVELS	**GROUP F**	**GROUP C**
T4	6.66%	3.33%
T5	23.33%	0
T6	40%	3.33%
T7	23.3%	20%
T8	6.6%	50%

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T9	0	13.33%

Table 10: Highest level (HL) SB

In our study, we found that, in group F, 40% of patients achieved a maximum level of SB at T6, followed by 23.3% at T5 and T7, and in group C, 50% of patients achieved a maximum level of SB at T8, followed by 20% at T7 (Table 10).

	GROUP F	**GROUP C**
Mean ± SD	52.77 ± 8.39	57.13 ± 15.7
p value	**0.001**	

Table 11: D of 2 segment regression time (SRT)

In our study , we found that by using unpaired t-test , DO-2SRT statistically significant difference awas seen as p value was 0.001 at mean difference of 4.36 min (Table 11).

	GROUP F	**GROUP C**
Mean ± SD	62 ± 19.74	78 ± 28.76
p value	0.142	

Table 12: D-SB

In our study, we found that, by using an unpaired t-test on comparing D between 2 groups, the p value was 0.142, i.e., non-statistically significant (Table 12).

	GROUP F	**GROUP C**
Mean ± SD	78.2 ± 14.75	80.6 ± 24.14
p value	0.059	

Table 13: D-MB

In our study ,we found that by using unpaired t-test , on comparing D between 2 groups, the p value was 0.059 ,i.e. non-stastistically significant (Table 13).

	GROUP F	**GROUP C**
Mean ± SD	100.97 ± 18.92	27.76
p value	**0.042**	

Table 14: D of analgesia(A)

In our study, we found that, using an unpaired t-test, DOA was statistically significant, with a p value of 0.042 at a mean difference of 8.2 min (Table 14).

Time	**Group F**	**Group C**	**p value**
Pre-operative	87.2±17.14	79.33±8.98	
0 min	87.20±17.393	82.40±14.989	0.257
5 min	89.23±15.536	85.03±15.650	0.301

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10 min	92.23±17.043	84.10±13.760	0.047
15 min	91.90±16.622	83.60±17.579	0.065
30 min	89.33±14.255	79.13±18.078	0.018
45 min	90.20±13.257	78.10±15.096	0.002
60 min	89.27±13.922	75.60±13.922	0.000
75 min	87.13±13.480	76.40±10.324	0.001
90 min	85.67±13.857	76.93±11.928	0.011

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig	Partial Eta Squared
Intercept	3868251.141	1	3868251.141	2589.85	0.000	0.978
Group	10899.030	1	10899.030	7.297	**0.009**	0.112
Error	86629.830	58	1493.618			

Table 15: HR at specific time interval (STI)

In our study ,we found that on comparing PR at STI statistically significant variation were observed at 30min, 45min, 60min ,75min& 90min as p value was 0.047, 0.018, 0.002, 0.001, 0.011 respectively (Table 15).

Time	**Group F**	**Group C**	**P value**
Pre-operative	88.34±9.29	101.04±7.41	
0 min	88.233±10.5682	99.922±6.8558	0.000
5 min	79.811±9.1223	90.856±7.5097	0.000
10 min	75.478±8.1291	86.133±10.4759	0.000
15 min	79.267±10.2016	83.911±12.5594	0.121
30 min	85.867±12.3331	80.889±11.9857	0.118
45 min	90.567±9.6859	85.233±14.1971	0.095
60 min	91.711±8.8663	87.711±14.3270	0.199
75 min	88.844±10.0526	90.644±12.0871	0.533
90 min	90.422±10.3331	92.222±9.1414	0.478

Transformed Variable: Average

Source	**Type III**	**df**	**Mean**	**F**	**Sig**	**Partial Eta**

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	Sum of Squares		Square			Squared
Intercept	4096254.943	1	4096254.943	6694.64	0.000	0.991
Group	1244.173	1	1244.173	2.033	0.159	0.034
Error	35488.501	58	611.871			

Table 16: MAP at STI

In our study, we found that on comparing MAP at STI, significant variation was observed at 0 min, 5 min, and 10 min, as the p value was 0.000 (Table 16).

DISCUSSION

Lee et al.,[8] in 2008 did a dose-deciding study and concluded that 35 and 40 mg of 2% chloroprocaine resulted in a spinal block and faster ambulation. Kopacz et al.,[9] in their study, concluded that spinal 2% chloroprocaine 20mg and 30mg doses can produce sensory anesthesia adequate for brief surgical produces. A 10-mg-mgse was considered a no-effect dose. In this study, we have used 1% chloroprocaine 25mg with adjuvants fentanyl 25 mg or 30 mg clonidine to achieve adequate surgical anesthesia for surgeries lasting up to 90 minutes.

	Current study		Vath et al.[10] (2%CP 40mg+ Fentanyl 20 mcg)	Vaghadia et al.[11] (1% CP 40mg+ Fentanyl 12.5mcg)	Davis et al.[12] (2%CP 40mg+ Clonidine 15mcg)
	Group F	**Group C**			
Onset of sensory block(mins)	8.5±1.5	9.67±3.9	-	4	-
Highest level of sensory block (mins)	12.4±3 T6(T4-T8)	6.7±2.7 T7(T4-T10)	21±11 T5(T3-T7)	20 T7-T8	T8(T4-T11)
2 segment regression time (mins)	52.7±8.3	57.1±15.7	48±8	-	-
Duration of sensory block (mins)	62±19.7	78±28.7	Reg to L1-77±7 Complete regression-104±7	-	Reg to L1-76±11 Complete regression-131±15
Duration of analgesia	100.9±18.9	92.7±27.7	-	-	-

Table 17: Comparison between studies (SB)

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	Current study		Vath et al.[10] (2%CP 40mg+ Fentanyl 20 mcg)	Vaghadia et al.[11] (1% CP 40mg+ Fentanyl 12.5mcg)	Davis et al.[12] (2%CP 40mg+ Clonidine 15mcg)
	Group F	**Group C**			
Onset of motor block (mins)	9.7±2.6	6.7±2.7	-	-	-
Duration of motor block (mins)	78.2±14.7	80.6±24.1	81±16	54	79±19

Table 18: Comparison between different studies (MB)

Hemodynamic(H) Parameter

In our study we found that, on comparing the HR between the two groups, significant variations were observed between the two groups. When compared at STI, significant variations were observed from 30 minutes to 90 minutes. On comparing the MAP, significant variations were not observed between the two groups. Studies haven't mentioned hemodynamic variations in the use of CP.

Adverse Effect

In our study, we found that intra-operative hypotension was observed in 6 patients in group C and 3 patients in group F, which was statistically significant. 2 (33%) out of 6 patients receiving clonidine required active intervention. The incidence of Bradycardia was observed in 2 patients in the clonidine group and 1 patient in the fentanyl group. One patient in the clonidine group required active intervention with Inj. Atropine 0.6 mg/IV. Similar adverse effects were seen in previous studies. (39,47) Pruritis was seen with the use of fentanyl and did not require any active intervention.

CONCLUSION

It has been observed that the utilization of low-dose (1%) CP in conjunction with either F or CL as an adjuvant is advantageous in procedures with a duration of less than 90 minutes. The combination of CP with F demonstrated a faster onset of SB and a longer DOA when compared to the other combination. The administration of CL has been found to be correlated with an increased likelihood of experiencing AE, such as hypotension and bradycardia. Conversely, the use of F has been linked to a higher probability of developing pruritis.

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