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Comparison of Clonidine versus Fentanyl as an Adjuvant to Intrathecal Ropivacaine for Infra Umbilical Surgeries

G. Gokulakrishnan , B. Kala*

Department of Anaesthesiology, Pain Medicine And Critical Care, SreeBalaji Medical College & Hospital Affiliated to Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

***Corresponding author e-mail id:**

kala.b@bharathuniv.ac.in

Abstract

The present study compares the efficacy of Clonidine and Fentanyl as an adjuvant to Ropivacaine in spinal anaesthesia in infra-umbilical surgeries in terms of block characteristics, quality of anaesthesia, hemodynamic parameters and complications. Block characteristics includes, onset of sensory and motor blockade, duration of sensory and motor blockade, maximum dermatome level of sensory blockade and the time taken to attain this maximum height. Non-invasive blood pressure, heart rate, oxygen saturation were the hemodynamic parameters compared. Quality of anaesthesia was compared by the sedation scores and time for rescue analgesics. This prospective double blinded randomized study was conducted in 100 patients between ages 18-65 years and ASA I & ASA II status who were undergoing elective infra-umbilical surgeries of duration less than or equal to 120 minutes under spinal anaesthesia. Group RC (n=50) received 30 micrograms of Clonidine to 2.5 ml (18.75 mg) of 0 75% isobaric Ropivacaine& group RF (n=50) received 25 micrograms of Fentanyl to 2.5 ml (18.75 mg) of 0.75% of isobaric Ropivacaine.

Keywords : Ropivacaine, analgesics, opioids, clonidine, sepsis, sensory and fentanyl

1. Introduction

The most important duty of an anaesthesiologist lies in providing relief from pain throughout the intra operative period as well as extending this pain relief to the post operative period. Regional anaesthesia, particularly Spinal anaesthesia has emerged among

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anaesthesiologists world-wide as a technique mainly due to its reliability, cost effectiveness, muscle relaxation and its prolonged post operative analgesia[1]The first planned Spinal Anaesthesia for surgery was performed by August Bier on 16th August 1898, in Kiel in Germany, when he injected 3ml of 0.5% cocaine solution into the sub-arachnoid space of a 34 year old labourer. After using it in 6 patients, he and his assistant Hildebrandt injected cocaine into each others' subarachnoid space to experiment further.[2]Since the first administration of spinal anaesthesia, various drugs have been used over the period of time in search of an ideal drug that provides an excellent surgical anaesthesia and also free of inadvertent side effects.

Traditionally, Bupivacaine, a local anaesthetic, belonging to amide class, is commonly being used for spinal anaesthesia. Bupivacaine has a prolonged motor block and in high doses may lead to myocardial depression, heart blocks, dysrrhythmias and toxicity of the central nervous system. [3,4]. It has also been observed that cardiac resuscitation is more difficult and refractory after Bupivacaine induced cardiovascular collapse.[5,6].In this fast moving world, necessity for early ambulation, quicker and complete recovery with minimal side effects has risen. Ropivacaine, a relatively newer local anaesthetic, is increasingly gaining acceptance for spinal anaesthesia. The total duration of motor and sensory block, two segment regression time and time for urination are shorter for Ropivacaine [7,8]. It is thus justified in using Ropivacaine for ambulatory surgeries. In addition, Ropivacaine has a lesser cardiotoxic and neurotoxic potential [9,10] and has a good hemodynamic stability[11]. Owing to these properties, Ropivacaine is said to possess a better safety margin.

Ropivacaine, used in spinal anaesthesia provides adequate anaesthesia intra- operatively and also in the immediate post operative period, but when its effect wears off, the patient may start to experience pain. Hence various adjuvants have been tried in spinal anaesthesia to improve its quality of anaesthesia and analgesia and extending it into the post operative period. The adjuvants also reduce the overall dose of local anaesthetic required.Opioids have been the standard choice of adjuvant in spinal anaesthesia due to their synergistic effects whilst not increasing the sympathetic blockade further[12,13,14]. Fentanyl, a lipophilic opioid is commonly used as an adjuvant andprovides a good quality of intra-operative and post operative analgesia with good hemodynamic stability. However opioids are known for their side effects including pruritus, urinary retention and catastrophic delayed respiratory depression [15].

Due to the above mentioned effects, non-opioid adjuvants came into use as adjuvant for spinal anaesthesia. Centrally acting α2 agonists have been used as adjuvant to improve the quality

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of anaesthesia and analgesia, particularly Clonidine which is an partial agonist at α2 receptor. When Clonidine is used at appropriate dose in spinal anaesthesia as adjuvant to Ropivacaine, it prolongs the duration of intraoperative anaesthesia and postoperative analgesia, whilst still making it possible to ambulate the patient [16].

This study was conducted to compare the efficacy of Clonidine and Fentanyl as adjuvants to intrathecalRopivacaine in terms of quality of surgical anaesthesia and analgesia, hemodynamic stability and side effects, while maintaining the advantages of Ropivacaine in terms of its cardiovascular and neurological safety and possibility of early ambulation.

2. MATERIALS AND METHODS

This study was conducted in SreeBalaji Medical College and Hospital, Chennai, between December 2017 to December 2018 in 100 patients. The study was conducted after obtaining institutional ethics committee approval. Written and informed consent was taken from all patients who were included in the study in their own language.This was a prospective, randomized, double blinded study. 100 patients were divided into 2 groups of 50 each. Patients were randomly allotted to either of the group by draw of lots

Group RC- 50 patients received 30 µg of Clonidine added to 2.5 ml of 0.75% isobaric Ropivacaine (18.75 mg) diluted with normal saline to make total volume of 3 ml.

Group RF- 50 patients received 25 µg of Fentanyl added to 2.5 ml of 0.75% isobaric Ropivacaine (18.75 mg) to make the final volume being 3 ml.

The total volume of injected solution was 3 ml in both the groups. All solutions were prepared under aseptic precautions in the operating room by a first anaesthesiologist not involved in the administration of subarachnoid block and observations of the patient were done by a second anaesthesiologist who was blinded of the drug administered.TheRopivacaine used in this study – 0.75% isobaric preparation was manufactured by NEON laboratories Ltd. The Fentanyl citrate used in this study was manufactured by Verve Health care limited. The Clonidine hydrochloride used in the study was manufactured by NEON laboratories Ltd. .

Inclusion criteria

Patients of either sex Age
between 18-65 years

American Society of Anaesthesiologists (ASA) class I

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and II

Elective surgeries involving below the umbilicus (infra umbilical surgeries)
Surgery duration less than or equal to 120 minutes

Exclusion criteria

Patient refusal- refusal for spinal anaesthesia (or) to be a part of the study
ASA class III and IV
Pregnantpatients
Patients with neurological disease
Spinaldeformity
Allergy to local anaesthetic
Coagulopathies
Sepsis
Any other contraindications to spinal anaesthesia

Preoperative evaluation

Routine preoperative assessment was done for the patients involved in the study which included thorough history of the patient and general physical examination, systemic examination, airway and spine assessment. Blood investigations were done, chest X ray and Electrocardiogram was done. All the patients were explained in detail about the procedure to be done. On the morning of surgery, before shifting the patient to the operating theatre, baseline hemodynamic parameters, which included blood pressure, heart rate, oxygen saturation were recorded.

Pre procedure checklist

After ensuring the functioning of suction, operating table position, presence of difficult airway equipments, anaesthetic and resuscitative drugs, resuscitative equipments, oxygen supply and properly working anaesthesia workstation, the patient was shifted inside the operating room.Upon shifting the patient to the operating table, minimum mandatory monitors like electrocardiogram, pulse oximeter, non-invasive blood pressure monitor, temperature monitor and end tidal carbon dioxide monitors were connected. 10ml/kg of Ringers' lactate was preloaded to the patient through an 18 G peripheral venous cannula.

Procedure details

Under strict aseptic precautions, patient in sitting position, the L2-L3 or L3-L4

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intervertebral space was identified and skin over the space was infiltrated with local anaesthetic 2% lignocaine. Using a 25 Gauge Quincke's spinal needle, subarachnoidspace was entered, which was confirmed by free flow of CSF after removing the stylet. One of the prepared drug solution was then injected without barbotage. After injecting, the patient was carefully made to lie supine immediately. After adequate level of sensory blockade, the surgeons were asked to proceed with the surgery.

PARAMETERS RECORDED

Hemodynamic parameters

1. Heart rate, non-invasive blood pressure (systolic blood pressure and diastolic blood pressure), oxygen saturation was monitored every minute for the first 5 minutes, every 5 minute till 15 minutes and every 15 minute till 120 minutes.
2. Any decrease in heart rate less than 60 beats/ minute was considered as bradycardia and was treated with 0.6mg atropine intravenously.
3. Hypotension was considered when systolic blood pressure was less than 90mmHg or fall in blood pressure >25% from the baseline value. It was treated with intravenous ephedrine 6mg bolus.

Sensory block

Sensory block was assessed by loss of sensation of temperature and pinprick sensation in the mid axillary line at 1 minute intervals. The study involving infra- umbilical surgeries, onset of sensory block was defined as the time taken from the injection of the intrathecal drug to sensory block at T10 level. The maximum height of sensory block is the maximum dermatomal level till which the sensory block occurs. The time taken to reach this maximum height of sensory block was noted. Duration ofsensory block was defined as the time from the onset of sensory block to T10 dermatome to the time taken for the sensory block to regress to L1 dermatome. Two segment regression time, which is the time taken to decrease from the maximum sensory dermatome level to 2 dermatome levels below, was recorded.

Motor block

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Motor block was assessed bilaterally by Modified Bromage Scale [16].

SCORE	MOTOR RESPONSE
0	No motor block; able to move leg freely
1	Inability to raise extended leg; able to move knees and feet
2	Inability to raise extended leg and move knee; able to move feet
3	Complete block of motor limb; no movement

Motor block was assessment was done at every 1 minute interval. Onset of motor block was defined as the time taken from intrathecal injection of the drug to attain modified bromage score of 3. Duration of motor block was defined as the time taken from the onset of motor block to complete recovery of motor block i.e. modified bromage score of 0.

Sedation levels

No intravenous sedative agents were given. Sedation scores were recorded by Chernik and Gilling sedation scores [15].

SCORE	SEDATION LEVEL
0	Wide awake
1	Calm and comfortable, responding to verbal command
2	Sleeping but arousable
3	Deep sleep, not arousable

Quality of anaesthesia

Quality of block was graded as

1. Adequate- no additional analgesic required during the surgicalprocedure.
2. Inadequate-additional analgesia required during theprocedure.
3. Failed-general anaesthesiarequired.

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If the level of analgesia was inadequate or failed, surgery was proceeded with balanced general anaesthesia and the patient was excluded from the study. Time taken for the requirement of first dose of analgesia was noted as the rescue analgesia time. The rescue analgesic used was diclofenac sodium 75 mg intramuscularly.

Presnece or absence of any complications

The presence or absence of any complications like hypotension, bradycardia, nausea/vomiting, shivering and pruritus were noted in both the groups. The statistical tool used was IBM SPSS Statistics for Windows, Version 26.0 was used for statistical calculation. Mean, standard deviation and p value are presented in the data. A p value of < 0.05 was considered as significant and p value <0.001 .

3. Results

100 patients were included in this double blinded study. They were randomly allotted into 2 groups of 50 each.

Group RC received 30 µg of Clonidine plus 2.5ml (18.75 mg) of 0.75% isobaric Ropivacaineintrathecally.

Group RF received 25 µg of Fentanyl plus 2.5ml (18.75 mg) of 0.75% isobaric Ropivacaineintrathecally.

Total volume of the injected solution was 3 ml in both the groups.

DEMOGRAPHIC DATA

Age distribution

In group RC, 28% of the patients were between ages 18-30 years, 40% were between 31-50 years of age and 32% were between 51-65 years of age. In group RF, 28% of the patients were between ages 18-30 years, 44% were between 31-50 years of age and 28% were between 51-65 years of age.

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			GROUP		Total	P VALUE
			CLONIDINE	FENTANYL		
AGE GROUP (in years)	18-30	Count	14	14	28	
		% within AGE GROUP	50.0%	50.0%	100.0%	
		% within GROUP	28.0%	28.0%	28.0%	
		% of Total	14.0%	14.0%	28.0%	
	31-50	Count	20	22	42	
		% within AGE GROUP	47.6%	52.4%	100.0%	
		% within GROUP	40.0%	44.0%	42.0%	
		% of Total	20.0%	22.0%	42.0%	
	51-65	Count	16	14	30	
		% within AGE GROUP	53.3%	46.7%	100.0%	
		% within GROUP	32.0%	28.0%	30.0%	
		% of Total	16.0%	14.0%	30.0%	
Total		Count	50	50	100	0.892
		% within AGE GROUP	50.0%	50.0%	100.0%	
		% within GROUP	100.0%	100.0%	100.0%	
		% of Total	50.0%	50.0%	100.0%	

Thus majority of the patients in both the groups were 31-50 years of age.

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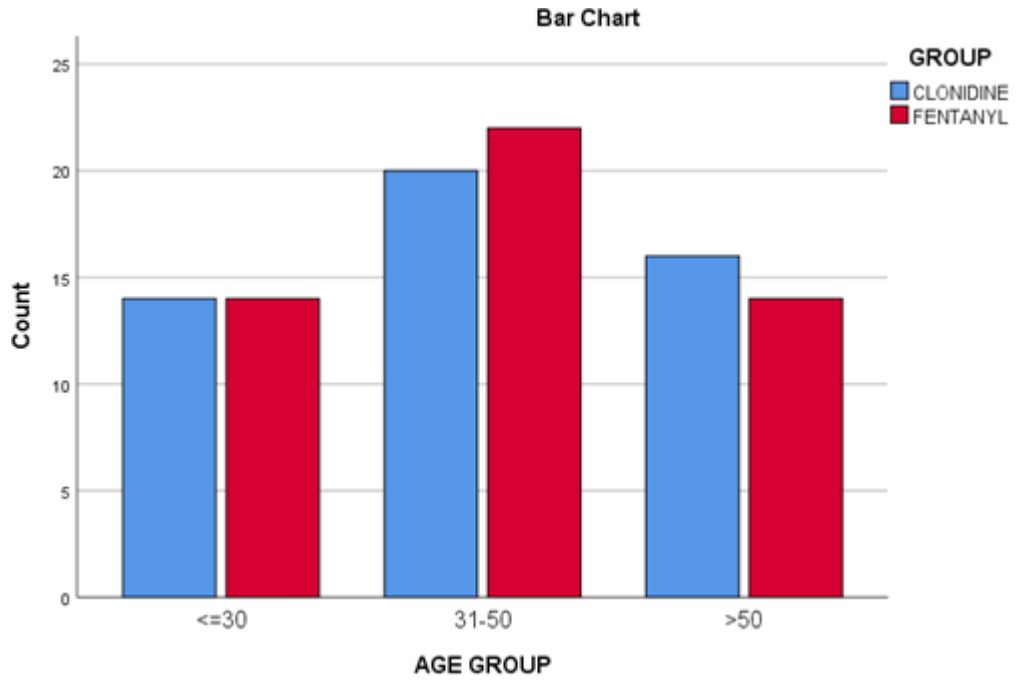

	GROUP	N	Mean	Std. Deviation
AGE (in years)	FENTANYL	50	40.66	12.010
	CLONIDINE	50	40.54	12.038

The mean age was found to be almost identical in both the groups. From the above data, it is observed that both the groups were statistically comparable with respect to age and no statistically significant differences were noted (P> 0.05).

Sex distribution

SEX DISTRIBUTION			GROUP		Total	P value
			CLONIDINE	FENTANYL		
SEX	FEMALE	Count	28	24	52	
		% within SEX	53.8%	46.2%	100.0%	
		% within GROUP	56.0%	48.0%	52.0%	
		% of Total	28.0%	24.0%	52.0%	

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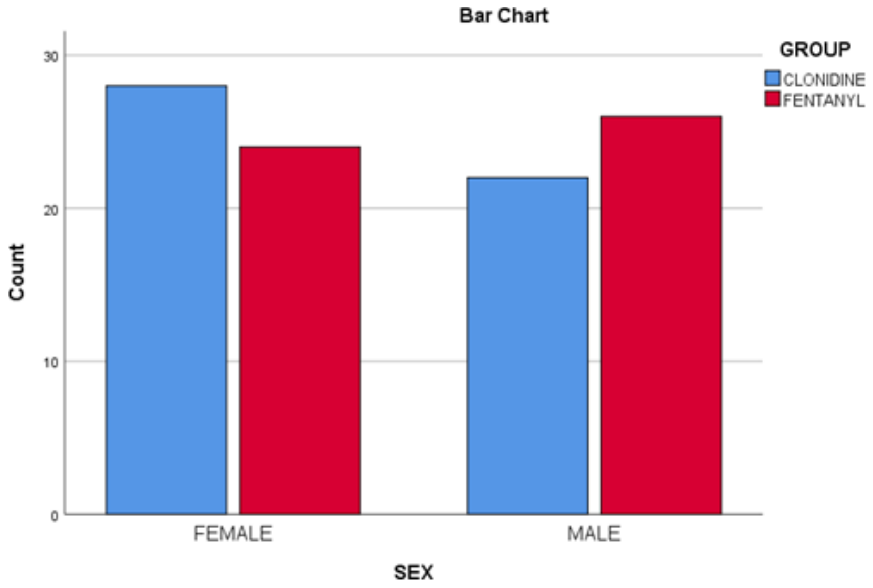
	MALE	Count	22	26	48	
		% within SEX	45.8%	54.2%	100.0%	
		% within GROUP	44.0%	52.0%	48.0%	
		% of Total	22.0%	26.0%	48.0%	
Total		Count	50	50	100	
		% within SEX	50.0%	50.0%	100.0%	0.423
		% within GROUP	100.0%	100.0%	100.0%	
		% of Total	50.0%	50.0%	100.0%	

In group RC, 56% were females and 44% were males. In group RF, 48% were females and 52% were males. In this study 52% were females and 48% were males.



From the above data, it is observed that both the groups were statistically comparable with respect to gender distribution and no statistically significant differences were noted (P> 0.05).

Height

	GROUP	N	Mean	Std. Deviation	P value
HEIGHT (in centimetres)	FENTANYL	50	159.84	7.081	0.614
	CLONIDINE	50	160.62	8.305	

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The mean height was 160.62 cms in group RC and 159.84 cms in group RF. From the above data, it is observed that both the groups were statistically comparable with respect to height and no statistically significant differences were noted (P> 0.05)

Weight

	GROUP	N	Mean	Std. Deviation	P value
WEIGHT (in kilograms)	FENTANYL	50	65.60	9.879	0.197
	CLONIDINE	50	63.10	9.370	

The mean weight in group RC was 63.10 kgs and 65.60 kgs in group RF. From the above data, it is observed that both the groups were statistically comparable with respect to weight and no statistically significant differences were noted (P> 0.05).

ASA Classification

			GROUP		Total	P value
			CLONIDINE	FENTANYL		
ASA	ASA 1	Count	34	36	70	0.662
		% within ASA	48.6%	51.4%	100.0%	
		% within GROUP	68.0%	72.0%	70.0%	
		% of Total	34.0%	36.0%	70.0%	
	ASA 2	Count	16	14	30	
		% within ASA	53.3%	46.7%	100.0%	
		% within GROUP	32.0%	28.0%	30.0%	
		% of Total	16.0%	14.0%	30.0%	
Total		Count	50	50	100	
		% within ASA	50.0%	50.0%	100.0%	
		% within GROUP	100.0%	100.0%	100.0%	

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	% of Total	50.0%	50.0%	100.0%	

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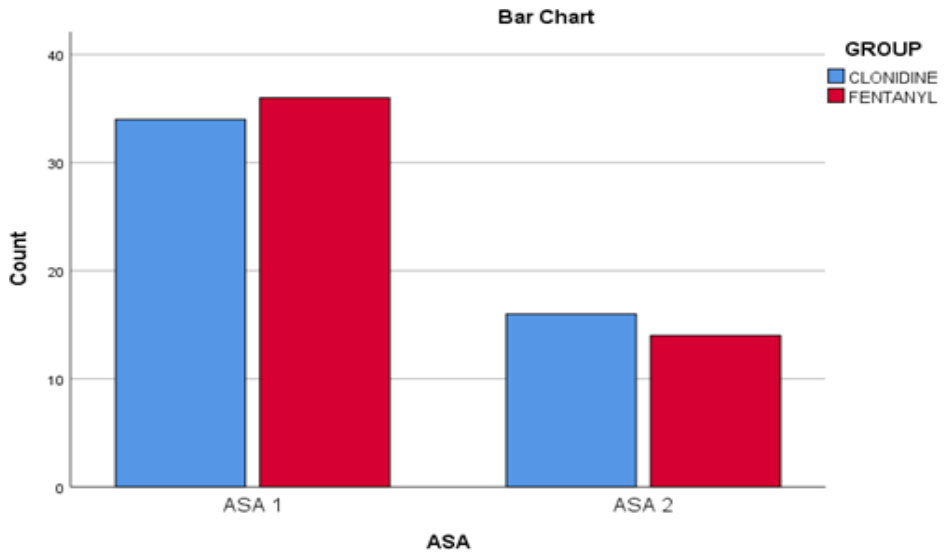

In this study majority of the patients- 70% belonged to ASA-I classification and 30% belonged to ASA-II classification. There was statistically no significant difference in the ASA classification between the two groups.

Discussion

Spinal anaesthesia has become the preferred technique for any surgeries that could be carried out with it, unless there are no contraindications. Introduction of local anaesthetic agents like Ropivacaine, which has shorter duration of action and better safety profile, has made it possible to give spinal anaesthesia for ambulatory surgeries. Adding various adjuvant to intrathecalRopivacaine will help to prolong the duration of blockade and improve the quality of analgesia and anaesthesia (15-17).

Ropivacaine has been reported to have better safety profile when compared to Bupivacaine. Fentanyl has been one of the common adjuvants which has been added to spinal anaesthesia. It has helped to prolong the duration of sensory blockade and provide better pain relief in the post operative period. However opioids are known for their undesirable effects like delayed respiratory depression and pruritus. Clonidine, is now being used as an adjuvant in spinal anaesthesia safely. When Ropivacaine is used intra thecally for a planned ambulatory surgery, when the duration of the surgery is unexpectedly prolonged, adding Clonidine will help to prolong the duration of sensory and motor block, thereby providing a good quality of anaesthesia and analgesia for the patient (18-20).

In this study, 0.75% of isobaric Ropivacaine was used for elective below- umbilicus surgeries and adjuvants compared were 25 micrograms of Fentanyl and 30 micrograms of Clonidine.

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Sensory block characteristics

The onset of sensory block was quicker in patients who received Fentanyl as adjuvant (mean -4.18 minutes) than in patients who received Clonidine as adjuvant (mean- 5.88 minutes). In a study conducted by RadheSharan and colleagues, the onset of sensory block was prolonged in patients who received Clonidine as an adjuvant when compared to patients who received Fentanyl as an adjuvant. Their findings are consistent with the present study. In one study conducted by Anita Chhabra and colleagues, the onset of sensory block was again delayed in patients who received Clonidine compared to patients who received Fentanyl as aduvants in spinal anaesthesia. These findings are consistent with the findings in our study. The maximum level of sensory was comparable in both the groups with Clonidine and Fentanyl. The time taken to reach this maximum level of sensory block was prolonged in Clonidine receivingpatients (21).

The duration of sensory block was prolonged in Clonidine receiving group (197.56 minutes) when compared to Fentany receiving group (173.54 minutes) which was statistically highly significant. In the study conducted by RadheSharan and colleagues [15], duration of sensory block was prolonged in patients who received Clonidine as compared to patients who received Fentanyl as spinal adjuvants. In another study conducted by Anita Chhabra and colleagues[18],duration of sensory block was prolonged in patients who received Clonidine as compared to patients who received Fentanyl as spinal adjuvants. Similar findings were observed in a study conducted by Ravanjit Singh and colleagues [19], where they compared Clonidine and Fentanyl as adjuvants to intrathecal Bupivacaine. In the group that receivedClonidine

to bupivacaine, the duration of sensory block was prolonged compared to group that received Fentanyl as adjuvant.

Motor block characteristics

Theonsetofmotorblockwascomparableinboththegroups.Thedurationof motorblockwasprolongedsignificantlyingroupthatreceivedClonidine(mean)The time to complete recovery of motor block was 153.2 ± 19.9 min. Similar findings were observed in a study conducted by RadheSharan et al., where the patients who received Clonidine had prolonged motor block when compared to patients who received Fentanyl as an adjuvant to intrathecalRopivacaine (22-25).

Hemodynamic parameters

There was no clinically significant hypotension occurring in both the groups probably attributed to the hemodynamic safety profile of Ropivacaine. Systolic blood pressure was lower in the Clonidine group when compared to Fentanyl group which was statistically significant. Similar findings were observed in a study conducted by Anita Chhabra et al., and in another study conducted by RadheSharan et al.,. Bradycardia occurred in Clonidine group

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in two patients whereas bradycardia occurred in one patient in Fentanyl group. The fall in heart rate was more profound in Clonidine group which was statistically significant when compared to Fentanyl group. Similar findings were observed in a study conducted by Anita Chhabra et al., oxygen saturation was comparable in both thegroups (25).

Quality of anaesthesia

88% of the patients in Clonidine group had sedation scores between 1 to 2 whereas 32% of the patients in Fentanyl group had sedation scores between 1 to 2. In a study conducted by Anita Chhabra et al., 80% of patients in Clonidine group was well sedated, which is a consistent finding with our study. Similar findings were observed in a study conducted by Ravanjit Singh and colleagues, where patients who received Clonidine were more sedated than patients who received Fentanyl. It is a desirable feature as it keeps the patient calm and comfortable.

The time for rescue analgesia was prolonged significantly in the clonidine group (mean – 317.20 minutes) when compared to the Fentanyl group (mean – 267.20 minutes). In a study conducted by Anita Chhabra and colleagues, similar findings were observed – Clonidine group had a prolonged analgesia time of 354 minutes (mean) whereas Fentanyl group had analgesia time of 234 minutes (mean). In another study conducted by Ogun et al., time for request of first analgesia was 360 minutes (mean) when 30 micrograms of Clonidine was added to 15 mg of intrathecalRopivacaine. This finding is consistent with our study. In a study conducted by Yegin et al [11]., the time for request of first analgesia was found to be 210 minutes (mean) when 25 micrograms of Fentanyl was added to 18 mg of intrathecalRopivacaine. This finding is consistent with ourstudy.

4. CONCLUSION

Addition of either Fentanyl or Clonidine to intrathecalRopivacaine improved the quality of anaesthesia for infra-umbilical surgeries. In this study, addition of Clonidine was found to have advantage over addition of Fentanyl to Ropivacaine, with regards to prolonged sensory & motor blockade and duration for rescue analgesia and patient comfort.Although close monitoring for hypotension and bradycardia is warranted when using Clonidine, an intrathecal dose of 30 micrograms or lesser can be used safely without hindering the advantage of early ambulation when Ropivacaine is used in spinalanaesthesia.

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Ethical approval: The study was approved by theInstitutional Ethics Committee

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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