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## Comparative study of intrathecal fentanyl and clonidine as adjuvants to hyperbaric bupivacaine under spinal anaesthesia in infraumbilical surgeries

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### Abstract

**Background:** Opioids are commonly used neuraxial adjuvants with local anaesthetics in subarachnoid block (SAB) for prolongation of analgesia, however Clonidine has shown to improve the quality of blockade without any neurotoxicity. This study assess the quality of SAB using intrathecal fentanyl and clonidine with bupivacaine in infraumbilical surgeries.

**Methods:** After obtaining ethical clearance and informed consent 80 patients were randomly allocated into 2 groups, Group F received 15µg fentanyl and group C received 30µg clonidine with 12.5mg hyperbaric bupivacaine each. The onset time to reach peak sensory and motor level, 2 segment regression time, total duration of motor and sensory blockade, time for first rescue analgesia, hemodynamic changes and side effects were recorded.

**Results:** The patients in group C had significantly prolonged sensory and motor blockade and less and delayed requirement of rescue analgesic than in group F.

**Conclusion:** Intrathecal clonidine as adjuvant is better than fentanyl as it prolongs motor and sensory block and reduced demand of rescue analgesic.

**Keywords:** Fentanyl, clonidine, adjuvant, spinal anaesthesia

### Introduction

Subarachnoid anaesthesia is the most popular as well as effective technique for infraumbilical surgeries. It provides fast onset and effective sensory and motor blockade. For decades lignocaine had been the local anaesthetic of choice for spinal anaesthesia. Its advantages are rapid onset of action and good motor block manifested as good muscle relaxation. Its use was limited by its short duration of action and has been implicated in transient neurologic symptoms and cauda equine syndrome following intrathecal injection [1, 2]. Bupivacaine is three to four times more potent than lignocaine [3].

Lower abdominal and lower limb surgeries may be performed under local, regional or general anaesthesia. Spinal block is still the first choice because of its rapid onset, superior blockade, lower risk of infection, less failure rates and cost effectiveness but has drawbacks of shorter duration of block and less post operative analgesia. Local anaesthetic bupivacaine is the commonest agent used for spinal anaesthesia but its relatively shorter duration of action may lead to early analgesic intervention in post-operative period [4]. Many adjuvants to local anaesthetic have been used for intraoperative as well as post operative analgesia.

Opioids are commonly used as intrathecal adjuvants to improve the quality of intra operative analgesia and prolong it in post-operative period without significant motor or autonomic blockade<sup>5</sup>. Side effects such as pruritis, nausea, vomiting, urinary retention and delayed respiratory depression have prompted further research towards non opioid analgesia with less serious side effect [3].

Clonidine, a selective partial alpha adrenergic agonist is being evaluated as an adjuvant to intrathecal local anaesthetics and has proven to be a potent analgesic, free of opioid related side effects [6]. It is known to increase both sensory and motor blockade of local anaesthetics in various surgical procedures without any significant side effects. When bupivacaine is combined with clonidine intrathecally, complete surgical anaesthesia could be obtained along with intra and post-operative pain relief with fewer side effects.

This study was conducted to evaluate and compare the characteristics of spinal block and its side effects in adult patients undergoing infraumbilical surgeries who received a subarachnoid block with bupivacaine with either fentanyl or clonidine.

Our aim was to study the quality of subarachnoid block using intrathecal adjuvants fentanyl and clonidine with hyperbaric bupivacaine in terms of

1. Onset and duration of sensory and motor blockade following intrathecal administration of the studied drugs.
2. Hemodynamic variations, if any, following intrathecal administration of fentanyl or clonidine with hyperbaric bupivacaine.
3. Side effects of the drugs if any.

### Methodology

After approval from institutional ethics committee, this prospective randomized double blind study was conducted from November 2016 to May 2018. Those patients who were posted for infraumbilical surgeries who gave written informed consent of either sex in the age group of 20-60 years with ASA physical status I and II weighing 50-80 kg with height between 150cm to 190cm were included in the study. Patients with allergy to local anesthetics, opioids and clonidine, Contraindications to spinal anaesthesia like raised intracranial tension, progressive neurodegenerative disorder, CNS infections, local infections, Spine deformities and patients with uncontrolled diabetes mellitus, hypertension, recent myocardial infarction, Pregnancy, Psychiatric disorder, hypovolaemic shock, Bleeding diathesis and coagulopathy were excluded from the study.

Preoperative evaluation of the patient was done on the day before surgery. After explaining the procedure, written and informed consent was obtained. Patient was advised overnight fasting and were premedicated with tablet *al.prazolam* 0.5 mg the night before and on the day of surgery. In the operating room, intravenous line was secured with 18G cannula and patients were preloaded with ringer's lactate solution at 15ml/kg. Monitors including pulse oximeter, noninvasive arterial blood pressure, electro cardio graph were connected to the patient and baseline vitals recorded.

The patients were randomly assigned to one of the two group with 40 patients receiving one of the following for the subarachnoid block:

Group F (n=40) - Bupivacaine (0.5% H) 2.5ml with fentanyl 15 µg.

Group C (n=40) - Bupivacaine (0.5% H) 2.5ml with clonidine 30 µg.

Under aseptic precautions with patient in lateral position, 25G Quincke spinal needle introduced into L3-L4 space, after confirming clear flow of cerebrospinal fluid and negative aspiration for blood, 3 ml of test drug injected intrathecally. Intraoperatively, vital parameters like heart rate, non-invasive blood pressure, percentage of oxygen saturation (SPO2) were recorded every 2 minute for the first 10 minutes, then every 5 minutes till 1 hour of surgery and then every 15 minutes till the end of surgery. Postoperatively, every 1 hr till the patient complaints of pain.

Alteration in the hemodynamic parameters such as hypotension was treated with intravenous fluids and injection mephenteramine 6mg intravenously and bradycardia was treated with injection Atropine 0.6mg intravenous bolus. Any adverse events like nausea, vomiting, pruritis, urinary retention etc., were noted and treated accordingly.

### Efficacy parameters were assessed as follow

1. Assessment of sensory blockade was tested by pin prick test using hypodermic needle and the time of onset, highest level of sensory blockade, time for 2 segment regression of sensory level, duration of sensory block noted.
2. Duration of motor blockade was assessed by Modified Bromage Scale
3. Pain intensity was measured using visual analog scale (VAS)
4. Sedation was assessed with Ramsay Sedation Scale and recorded. Score of 4 and above is considered as sedated.
5. Duration of complete analgesia was assessed from the time of onset of analgesia till the appearance of pain for first time (first rescue analgesic). Rescue analgesia provided with interventional analgesics.
6. Any complications occurred in the first post-operative week that was communicated to us was documented.

Sample size was estimated by using the difference in Mean duration of Motor block between Group F and Group C from the study Yogesh Tilkar *et al.* as  $166.5 \pm 11.61$  min and  $177 \pm 23.69$  min. using these values at 95% Confidence limit and 80% power sample size of 40 was obtained in each group. Data was entered into Microsoft excel data sheet and was analyzed using IBM SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. P value (Probability that the result is true) of  $<0.05$  was considered as statistically significant after assuming all the rules of statistical tests.

### Results

All the patients included in the study received the assigned intervention and were followed up till the end of study. There were no exclusions or drop outs. Patient demographic characteristics were comparable in both groups (age, gender, weight, height, BMI). Number of patients belonging to ASA class I and II were uniformly distributed between both the groups. There was no significant difference in mean duration of surgery between two groups. In Group F, mean Duration of Surgery was  $60.1 \pm 19.2$  min and in Group C was  $68.5 \pm 25.5$  min.

Mean Onset of sensory blockade at L1 in Group F was  $72.63 \pm 17.32$  secs and in Group C was  $76.63 \pm 25.23$  Secs. There was no significant difference in mean onset of sensory blockade between two groups. Mean Onset of sensory blockade at T10 in Group F was  $132.05 \pm 18.42$  secs and in Group C was  $139.75 \pm 25.19$  Secs. There was no significant difference in mean onset of sensory blockade between two groups.

Mean Onset of Motor blockade in Group F was  $142.63 \pm 24.15$  secs and in Group C was  $147.00 \pm 27.43$  Secs. There was no significant difference in mean onset of Motor blockade between two groups.

In Group F, 2.5% had T4 level, 30% had T6 level, 42.5% had T8 level and 25% had T10 level. In Group C, 0% had T4 level, 40% had T6 level, 42.5% had T8 level and 17.5% had T10 level. There was no significant difference in Max

Height of Sensory Blocked between two groups. In Group F, mean Two Dermatome Regression was  $47.5 \pm 7.6$  min, mean Duration of Sensory Blockade was  $205.0 \pm 28.5$  min and mean Duration of Motor Blockade was  $178.7 \pm 29.3$  min. In Group C, mean Two Dermatome Regression was  $56.0 \pm 10.3$  min, mean Duration of Sensory Blockade was  $229.3 \pm 26.8$  min and mean Duration of Motor Blockade was  $203.5 \pm 23.5$  min. There was significant difference in mean Two Dermatome Regression, mean Duration of Sensory Blockade and mean Duration of Motor Blockade between two groups.

In Group F, mean time taken for First Analgesic was  $213.25 \pm 30.75$  min and in Group C, mean time taken for First Analgesic was  $236.00 \pm 27.62$  min. There was significant difference in mean Time for First Analgesic between two groups.

In the study there was significant difference in mean Pulse rate between two groups from 4 min intra op period to 60 min intra op period between group F and Group C. At these intervals mean PR was significantly higher in Group F than in Group C. At other intervals there was no significant difference in mean PR between two groups. In the study there was significant difference in mean SBP between two groups from 4 min intra op period to 45 min intra op period between group F and Group C. At these intervals mean SBP was significantly higher in Group F than in Group C. At other intervals there was no significant difference in mean SBP between two groups.

In the study there was significant difference in mean DBP between two groups from 2 min intra op period to 40 min intra op period between group F and Group C. At these intervals mean SBP was significantly higher in Group F than in Group C. At other intervals there was no significant difference in mean DBP between two groups.

In the study there was significant difference in mean MAP

between two groups from 4 min intra op period to 30 min intra op period between group F and Group C. At these intervals mean MAP was significantly higher in Group F than in Group C. At other intervals there was no significant difference in mean DBP between two groups. There was no significant difference in mean SpO2 between two groups at all the intervals of follow-up.

In Group F, 2.5% had nausea and 10% had Pruritis. In Group C, 2.5% had Bradycardia and 5% had hypotension. There was no significant difference in side effects between two groups. In the study there was no significant difference in sedation score between two groups from at all the interval except at 24 hr.

**Table 1:** Demographic parameters of subjects in two groups

	Group				P value
	Group F		Group C		
	Mean	SD	Mean	SD	
Age in years	41.4	13.5	40.2	12.6	0.683
Weight in KG	61.4	8.5	63.3	8.5	0.316
Height in M	1.6	0.1	1.6	0.1	0.187
BMI	24.9	4.2	24.9	3.9	0.976

Patient demographic characteristics were comparable in both groups.

**Table 2:** ASA grade comparison between two groups

		Group			
		Group F		Group C	
		Count	%	Count	%
ASA	1	23	57.5%	21	52.5%
	2	17	42.5%	19	47.5%

$\chi^2 = 0.202, df = 1, p = 0.653$

Number of patients belonging to ASA class I and II were uniformly distributed between both the groups.

**Table 3:** Duration of surgery, Onset of Sensory and Motor Blockade between groups

		Group				P value
		Group F		Group C		
		Mean	SD	Mean	SD	
Duration of surgery		60.1	19.2	68.5	25.5	0.101
Sensory Blockade	@ L1	72.63	17.32	76.63	25.23	0.411
	@ T10	132.05	18.42	139.75	25.19	0.123
Onset of Motor blockade		142.63	24.15	147.00	27.43	0.451

There was no significant difference in mean duration of surgery between two groups.

There was no significant difference in mean onset of sensory and motor blockade between two groups.

**Table 4:** Max Height of Sensory Blocked comparison between two groups

		Group			
		Group F		Group C	
		Count	%	Count	%
Max Height of Sensory Blocked	T4	1	2.5%	0	0.0%
	T6	12	30.0%	16	40.0%
	T8	17	42.5%	17	42.5%
	T10	10	25.0%	7	17.5%

$\chi^2 = 2.101, df = 3, p = 0.552$

There was no significant difference in Max Height of Sensory Blocked between two groups

**Table 5:** Two Dermatome Regression, Total Duration of Sensory Blockade and Duration of Motor Blockade comparison between two groups

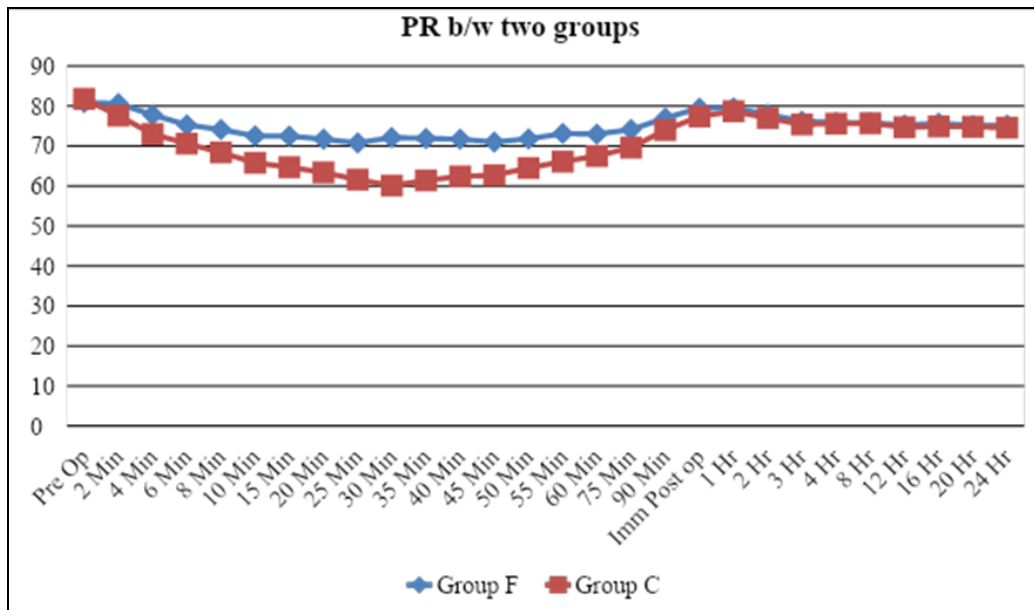
	Group				P value
	Group F		Group C		
	Mean	SD	Mean	SD	
Two Dermatome Regression	47.5	7.6	56.0	10.3	<0.001*
Total Duration of Sensory Blockade	205.0	28.5	229.3	26.8	<0.001*
Duration of Motor Blockade	178.7	29.3	203.5	23.5	<0.001*

There was significant difference in mean Two Dermatome Regression, mean Duration of Sensory Blockade and mean Duration of Motor Blockade between two groups

**Table 6:** Comparison of Time for First Analgesic between two groups

		Time for First Analgesic		P value
		Mean	SD	
Group	Group F	213.25	30.75	0.001*
	Group C	236.00	27.62	

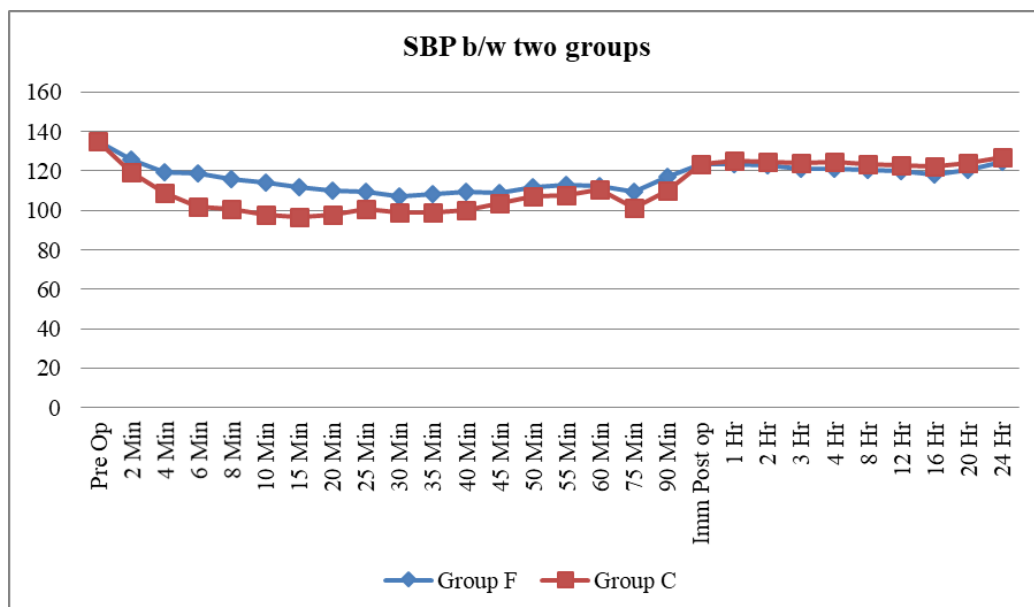
There was significant difference in mean Time for First Analgesic between two groups.



**Fig 1:** Line diagram showing Pulse rate comparison between two groups at different intervals of followup

In the study there was significant difference in mean Pulse rate between two groups from 4 min intra op period to 60 min intra op period between group F and Group C. At these

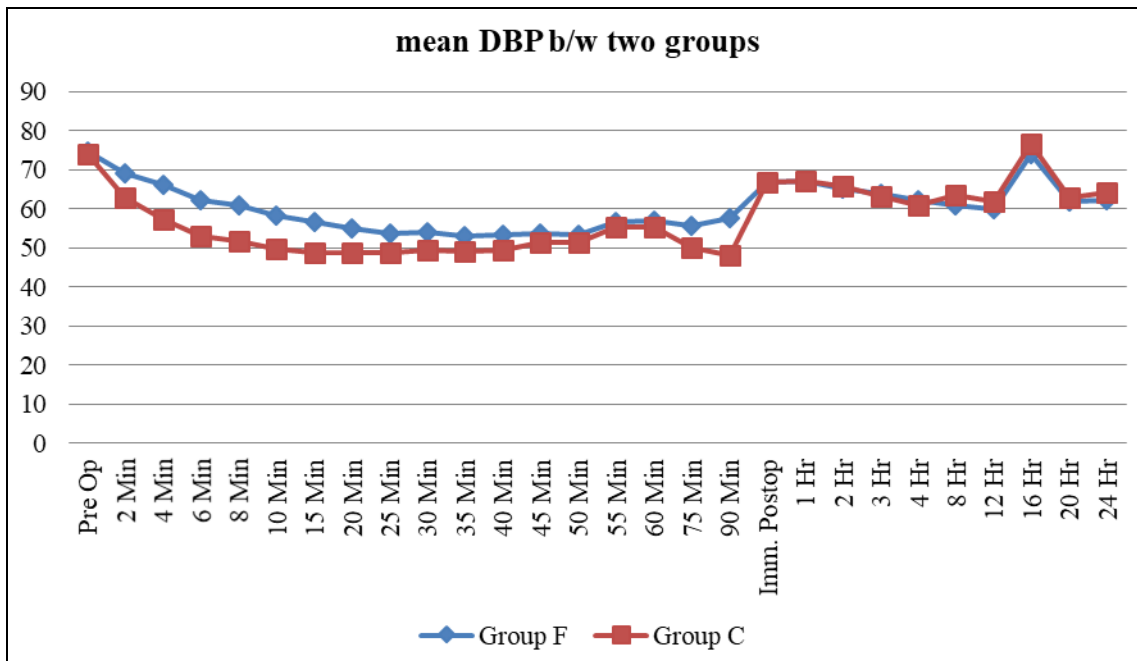
intervals mean PR was significantly higher in Group F than in Group C. At other intervals there was no significant difference in mean PR between two groups.



**Fig 9:** Line diagram showing SBP comparison between two groups at different intervals of followup

In the study there was significant difference in mean SBP between two groups from 4 min intra op period to 45 min intra op period between group F and Group C. At these

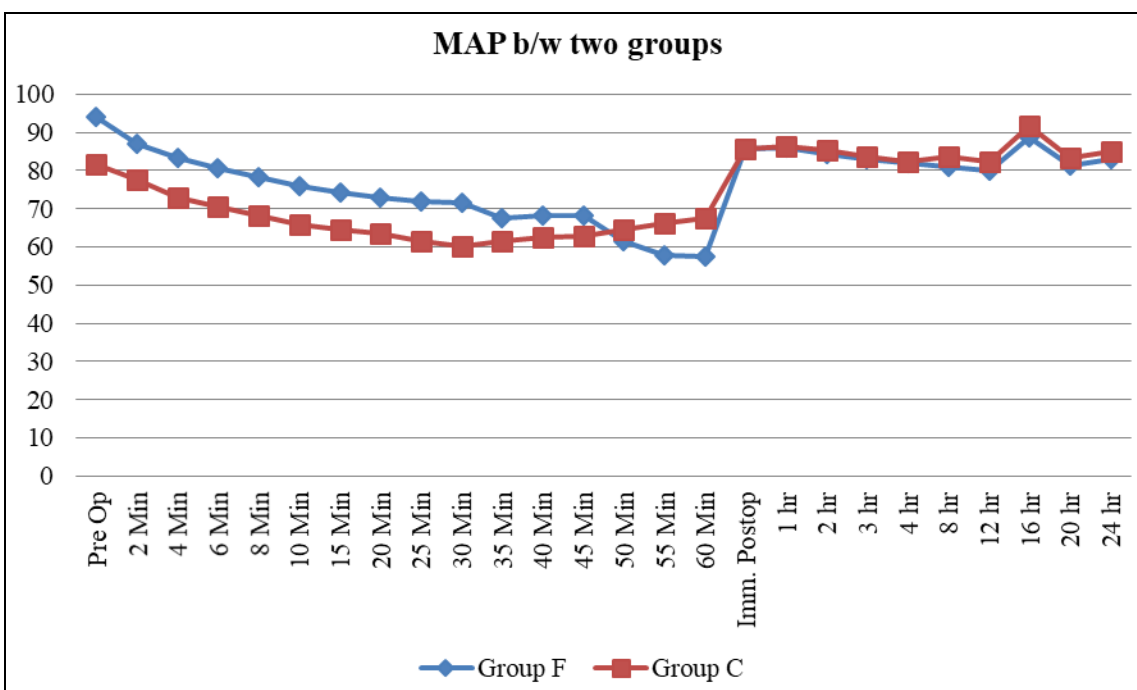
intervals mean SBP was significantly higher in Group F than in Group C. At other intervals there was no significant difference in mean SBP between two groups.



**Fig 10:** Line diagram showing DBP comparison between two groups at different intervals of followup

In the study there was significant difference in mean DBP between two groups from 2 min intra op period to 40 min intra op period between group F and Group C. At these

intervals mean SBP was significantly higher in Group F than in Group C. At other intervals there was no significant difference in mean DBP between two groups.



**Fig 11:** Line diagram showing MAP comparison between two groups at different intervals of followup

In the study there was significant difference in mean MAP between two groups from 4 min intra op period to 30 min intra op period between group F and Group C. At these intervals mean MAP was significantly higher in Group F than in Group C. At other intervals there was no significant difference in mean DBP between two groups.

**Discussion**

Subarachnoid blockade with bupivacaine is administered commonly for lower abdominal and lower limb surgeries. It provides effective pain relief in the initial postoperative

period. To address the problem of limited duration of action and to improve the quality of analgesia both intraoperative and postoperative, intrathecal opioids have been given in addition to bupivacaine.

Opioids are commonly used as intrathecal adjuvants to improve the quality of intra operative analgesia and prolong it in post-operative period without significant motor or autonomic blockade. Side effects such as pruritis, nausea, vomiting, urinary retention and delayed respiratory depression have prompted further research towards non opioid analgesia with less serious side effects. Clonidine, a

selective partial alpha adrenergic agonist is being evaluated as an adjuvant to intrathecal local anaesthetics and has proven to be a potent analgesic, free of opioid related side effects. It is known to increase both sensory and motor blockade of local anaesthetics in various surgical procedures without any significant side effects. Several studies have been done comparing opioids and different doses of clonidine in order to determine the most effective intrathecal administration with minimal side effects. Hence this study was done to evaluate the quality of subarachnoid block using intrathecal adjuvants clonidine and fentanyl with hyperbaric bupivacaine in terms of onset and duration of sensory and motor block, duration of analgesia, haemodynamic parameters and side effects if any.

We conducted a study comparing intrathecal fentanyl and clonidine as adjuvants to hyperbaric bupivacaine under spinal anaesthesia in infraumbilical surgeries, and found that there was no significant difference in mean onset of sensory and motor blockade between two groups. There was no significant difference in Max Height of Sensory Blocked between two groups. But there was significant difference in mean Two Dermatome Regression, mean Duration of Sensory Blockade and mean Duration of Motor Blockade between two groups. There was significant difference in mean Time for First Analgesic between two groups.

In the study there was significant difference in mean Pulse rate between two groups, mean PR was significantly higher in Group F than in Group C. There was significant difference in mean SBP, mean DBP, mean MAP between two groups, which was higher in Group F than in Group C. There was no significant difference in mean SpO<sub>2</sub> between two groups at all the intervals of followup. There was no significant difference in side effects between two groups.

Deepthi Agarwal, Manish Chopra *et al.* (2014) [8] hypothesised that addition of small doses of clonidine augments the spinal block levels produced by hyperbaric bupivacaine in elderly without affecting the side-effects of clonidine in these patients, and conducted a prospective, randomized, double-blind study. patients were allocated to three equal groups. Group C received 9 mg hyperbaric bupivacaine without clonidine while Group C15 and Group C30 received 15 µg and 30 µg clonidine with hyperbaric bupivacaine respectively for spinal anaesthesia. Results showed a significantly higher median block levels were achieved in Group C15 ( $P < 0.001$ ) and Group C30 ( $P = 0.015$ ) than Group C. Highest median sensory block level, the mean times for sensory regression to T12 level and motor block regression were statistically significant between Groups C15 and C and between Groups C30 and C. On comparison of fall in systolic blood pressure trends, there was no significant difference in the clonidine groups as compared with the control group. Hence concluded that Clonidine in doses of 30 µg facilitated the ascent of sensory level block to unexpectedly higher dermatomes for a longer time<sup>7</sup>. Similarly in our study there was no significant difference in mean onset of sensory and motor blockade between two groups. There was no significant difference in Max Height of Sensory Blocked between two groups. But there was significant difference in mean Two Dermatome Regression, mean Duration of Sensory Blockade and mean Duration of Motor Blockade between two groups.

Chopra P *et al.* (2014) conducted a prospective, randomized, double-blind study on 75 ASA grade I-II patients, who were scheduled for vaginal hysterectomy with pelvic floor repair

or non- descent vaginal hysterectomy under spinal anaesthesia. The patients received hyperbaric bupivacaine (2.3 ml) with fentanyl 15 µg (Group BF) or clonidine 30 µg (Group BC) or both fentanyl (15 µg) and clonidine (30 µg) (Group BCF). The total amount of intrathecal mixture was constant (2.8 ml) in all the groups. The duration of effective analgesia, mean time till two-segment regression, and duration of sensory and motor block were significantly longer in group BCF as compared to group BC ( $P \sim 0.002$ ), and in group BC as compared to group BF ( $P \sim 0.01$ ). The incidence of intraoperative pain and requirement of postoperative analgesics in the first 24 hours was significantly more in group BF as compared to the other groups ( $P \sim 0.01$ ). There was no difference in the hemodynamic profile between the groups. Hence concluded that Low-dose clonidine (30 µg) when added to a bupivacaine-fentanyl mixture increased the duration of effective analgesia and the duration of sensory and motor block in gynecological surgery. The incidence of intraoperative pain and requirement of postoperative analgesics was significantly less when clonidine was added to intrathecal bupivacaine with or without fentanyl<sup>8</sup>. Similarly in our study there was no significant difference in mean onset of sensory and motor blockade between two groups. There was no significant difference in Max Height of Sensory Blocked between two groups. But there was significant difference in mean Two Dermatome Regression, mean Duration of Sensory Blockade and mean Duration of Motor Blockade between two groups Tilkar Y *et al.* (2015) conducted a study on effect of adding clonidine versus fentanyl to intrathecal bupivacaine on spinal block and 90 patients were randomly divided into three groups of 30 patients each for lower limb orthopedic surgeries. Group A received intrathecal 15 mg hyperbaric bupivacaine and 1 ml normal saline, group B received 15 mg hyperbaric bupivacaine and 1 ml (50 µg) fentanyl, and group C received 15 mg hyperbaric bupivacaine and 1 ml (150 µg) clonidine. There was significant prolongation of duration of sensory ( $P = 0.0000001$ ) and motor block ( $P = 0.0000001$ ) was found in group C. Significant hypotension was found in group C ( $P < 0.05$ ) and the postoperative pain scoring chart (VAS chart) was  $1.07 \pm 0.87$  in group C and  $3.27 \pm 0.67$  in group B ( $P < 0.05$ ). Hence concluded that Intrathecal clonidine is associated with prolonged motor and sensory block, hemodynamic stability, and low postoperative pain score compared to fentanyl<sup>9</sup> similar to our study.

Routray SS, Raut K and co workers conducted a prospective randomized study in which eighty patients posted for lower limb orthopedic surgery were divided into two groups of forty each. Group C – Received intrathecal hyperbaric bupivacaine +50 µg clonidine, Group F – Received intrathecal hyperbaric bupivacaine + fentanyl 25 µg. Duration of postoperative analgesia, sensory and motor block characteristics, hemodynamic parameters, and side effects were recorded and analyzed and found that Time for first dose of rescue analgesic was delayed in Group C ( $510.84 \pm 24.10$  min) in comparison to Group F ( $434.95 \pm 19.16$  min) which was statistically significant ( $P < 0.001$ ). Duration of sensory and motor block was significantly prolonged in Group C compared to Group F ( $P < 0.001$ ). Sedation was more in Group C than Group F ( $P < 0.001$ ). Other block characteristics, hemodynamic, and side effects were comparable in both groups. Hence concluded that Intrathecal clonidine as adjuvant to hyperbaric bupivacaine

provided prolonged postoperative analgesia with more sedation in comparison to intrathecal fentanyl<sup>10</sup>. Similarly in our study there was significant difference in mean Time for First Analgesic between two groups.

## References

1. Richard Brull, Alan JR. MacFarlane Vincent W.S.Chan. Spinal, Epidural, and Caudal Anaesthesia. In: Ronald D. Miller editor. Miller's Anaesthesia 8th ed. Philadelphia Elsevier Saunders 2015, 1698-1699
2. Lennart Christiansson. Update on adjuvants in regional anaesthesia. Periodicum Biologorum UDC 2004.
3. Jacob AK, Kopp SL, Bacon DR, Smith HM. The History of Anesthesia. In: Barash PG, Cullin.BF, Stoelting RK, eds. Clinical Anaesthesia, 6th ed. Philadelphia: Lippincott Williams and Wilkins 2009, 3-26.
4. Larson MD. History of anaesthetic practice. In Miller's anaesthesia. Ed by Ronald D Miller. 6th ed. Churchill Livingstone 2005, 3-5.
5. Tony L Yaksh, Mark S. Wallace. Opioids, Analgesia, and Pain Management. In: Laurence L. Brunton, editor. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 12th ed. New York Mc Graw Hill 2011, 510
6. Dan Benhamou, Dominique Thorin, Jean Francois Brichant *et al.* Intrathecal clonidine and fentanyl with hyperbaric bupivacaine improves analgesia during cesarean section. *Anaesth Analg* 1998;87:609-13.
7. Deepthi Agarwal, Manish Chopra, Medha Mohta, Ashok Kumar Sethi. Clonidine as an adjuvant to hyperbaric bupivacaine for spinal anaesthesia in elderly patient undergoing lower limb orthopaedic surgeries, *Saudi J Anaesth* 2014;8(2):209-214
8. Chopra P, Talwar V. Low dose intrathecal clonidine and fentanyl added to hyperbaric bupivacaine prolongs analgesia in gynaecological surgery. *J Anaesthesiol Clin Pharmacol* 2014;30:233-7
9. Tilkar Y, Bansal SA, Agnihotri GS. A comparative study of intrathecal clonidine and fentanyl as adjuvants to bupivacaine in lower limb orthopaedic surgery-*Int J Med Sci public health* 2015;4:458-462
10. Routray SS, Raut K, Pradhan A, Dash A, Soren M. Comparison of intrathecal clonidine and fentanyl as adjuvant to hyperbaric bupivacaine in subarachnoid block for lower limb orthopaedic surgery. *Anaesth Essays Res* 2017;11:589-93.