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ORIGINAL RESEARCH

A randomized double blind comparative study of the effects of fentanyl and clonidine as additives to intrathecal hyperbaric bupivacaine for spinal anaesthesia

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ABSTRACT

Aim: To compare the effects of fentanyl 25microgram and clonidine 30 microgram as additives to 3 ml of 0.5 % hyperbaric bupivacaine for spinal anaesthesia in lower extremity orthopedic and urological surgeries.

Materials and methods: This prospective, randomized, double blind study was conducted on 60 adult patients of ASA physical status 1 & 2 in the age group of 20 years to 60 years, posted for elective lower limb and urological surgeries under spinal anaesthesia. Patients belonging to group BF received 3 ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.5 ml (25 microgram) fentanyl. Patients of group B received 3 ml (15 mg) of hyperbaric bupivacaine (0.5 + 0.2 ml (30 microgram) clonidine + 0.3 ml of normal saline. The following parameters were observed - onset and duration of sensory block, onset and duration of motor block, durations of complete and effective analgesia and any side effects associated with these drugs.

Results: The present study showed that the duration of sensory and motor block was prolonged with the addition of 30 microgram clonidine to intrathecal hyperbaric bupivacaine as compared to 25 micrograms of fentanyl, same as the duration of complete and effective analgesia. Both groups were comparable in hemodynamic stability and there were no significant adverse effects.

Conclusion: Compared to fentanyl 25 microgram, clonidine 30 microgram as additive to intrathecal hyperbaric bupivacaine for spinal anaesthesia, prolonged the duration of complete and effective analgesia, which was statistically significant

Keywords: Fentanyl, clonidine, Intrathecal hyperbaric bupivacaine, Effective analgesia

INTRODUCTION

More than a century has passed and even today, it is one of the most popular techniques for both elective and emergency surgical procedures particularly caesarean sections, lower abdominal surgeries, orthopedic and urological surgeries just to name a few[2]. Spinal anesthesia, defined, as 'the regional anesthesia obtained by blocking nerves in the subarachnoid space is a popular and common technique used worldwide. The advantages are awake patient, simple to perform, offers rapid onset of action, minimal drug cost, relatively

less side effects, reliable surgical analgesia and good muscle relaxation, which made this the choice of many a surgical procedure[3].

Spinal anaesthesia with lignocaine was highly popular earlier for short surgical procedures as it had a predictable onset and provided dense sensory and motor blockade of moderate duration. Unfortunately, some reports of neurotoxicity had cast doubts on the intrathecal use of lignocaine. In view of controversy and uncertainty surrounding the use of spinal lignocaine, hyperbaric bupivacaine (0.5 %) has replaced lignocaine as the gold standard drug for the safe conduct of spinal anaesthesia in recent times. Sensory and motor blockade is satisfactory. But its duration of action, though longer than that of lignocaine is limited.

Therefore, it forms a challenging forefront in clinical and research advances, where if one can enhance sensory blockade into postoperative period by combining the lowest dose of the drugs with longer duration of action and leastside effects, probably it may go a long way in alleviation of pain and suffering In order to extend intraoperative analgesia into postoperative period a number of spinal adjuvants such as opioids like morphine, fentanyl, alpha 2 agonists like clonidine and dexmedetomidine, anticholinergics like neostigmine and many other drugs have been added to prolong intrathecal bupivacaine action. However, each drug has its own limitations and a need for alternative methods or drugs always exist[4]. Intrathecal clonidine at the usual dose (1-2ug/kg)is associated with side effects such as hypotension and bradycardia. A few studies have focused on small doses (15ug to 37.5ug)to avoid these complications. As there are only a handful of studies comparing lower doses of intrathecal clonidine and fentanyl, the present study was undertaken to compare the effects of clonidine (30 microgram) and fentanyl (25 microgram) as additives to intrathecal hyperbaric bupivacaine (0.5 %) for spinal anaesthesia.

MATERIAL AND METHODS

A prospective randomized double blind controlled study from April 2015 to June 2016 at Sri Sathya Sai Institute of Higher Medical Sciences, Prashanthigram, Andhra Pradesh, Orthopedic and Urology Operation theatre Complex. 60 adult patients of physical status ASA grade I and2 in the age group of 20-60 years, posted for elective lower extremity orthopaedic or urological surgeriesunder spinal anesthesia.

Total sample size = 60 patients (30 in each group)

Group BF: Inj. Bupivacaine Hyperbaric 0.5% 3 ml + Fentanyl 25 µg (0.5 ml).

Group BC: Inj. Bupivacaine Hyperbaric 0.5% 3 ml + Clonidine 30 µg (0.2 ml) + 0.3 ml normal saline.

Sample size is calculated by considering two-sided significance level of 95%. Using results of the previous studies, group BF was taken as reference, which gives a sample size of 60.The calculation done with the formula[5]

Patients were randomly allocated into two groups by computer generated randomization chart.

INCLUSION CRITERIA

Patients aged between 20-60 yearswith ASA Grade-I and Grade-II, Weight between 50 to 70 kg, Height between 150 to 180 cmPatients scheduled to undergo elective lower extremity orthopedic and urological surgeries under subarachnoid block.

EXCLUSION CRITERIA

Patients physically dependent on alpha2 agonists, benzodiazepines and opioids, with gross spinal abnormality, localized skin infection, sepsis, Hemorrhagic diathesis or neurological diseases, with history of drug allergy, Pregnancy, with cardiac, pulmonary, hepatic or renal disorders and with peripheral neuropathy

Prior to the commencement, the study was approved by the Ethics and scientific Committee (Dissertation Committee), Sri Sathya Sai Institute of Higher Medical Sciences, Prashanthigram, Ananthapur Dist [Ref.No. SSSIHMS-PG/ACAD./15/] All the patients fulfilling selection criteria were explained about the nature of the study and intervention and a written informed consent was obtained from all the patients before enrollment. Detailed pre anesthetic evaluation including history, clinical examination, systemic examination of cardiovascular, respiratory and central nervous systems and examination of spine for deformity, infection was carried out.

The anesthetic procedure was briefly explained to the patient. An informed written consent was obtained from the patients. Routine investigations like haemogram, total leucocyte count, differential leucocyte count, ESR, complete urine examination, random blood sugar, electrocardiogram, chest x-ray, blood grouping, blood urea, serum creatinine, coagulation profile, liver function tests and serology was done. During the pre-anesthetic visit, every patient was familiarized with linear visual analog scale (VAS 0 = no pain and 10 = worst imaginable pain) Each patient's weight and height was also recorded.

All the patients were premedicated with tab Diazepam 5mg orally, on the night before surgery. No other pre-medication was administered before the start of the anaesthetic procedure and they were kept nil orally for 8 hours before surgery.

All resuscitation equipment’s like intubation trolley with airways, laryngoscopes, endotracheal tubes along with drugs like atropine, ephedrinre, were kept ready. The anesthesia machine was also checked along with the oxygen delivery system. Once the patient was shifted to the operating room, the patient was connected to the routinemonitors which included noninvasive blood pressure, pulse oximetry and 5-electrode electrocardiogram.

Baseline pulse rate, blood pressure, respiratory rate and SPO_2 were recorded. A wide bore intravenous access using a 18G IV cannula was obtained and secured. All patients were preloaded with 500m1 of Ringer's lactate prior to spinal anesthesia The patients were then put in sitting position. The study solutions were prepared in a 5 ml syringe by an anesthesiologist who then handed over the syringe in a coded form to the attending anaesthesiologist performing subarachnoid block. Clonidine was taken by using insulin syringe. Under strict aseptic precautions, lumbar puncture was performed by midline approach by using disposable Quincke's spinal needle (25G) at L3—L4 intervertebral space. Patients belonging to group "BF" were administered 3 ml (15 mg) of hyperbaric bupivacaine (0.5%) + 25mcg fentanyl (0.5m1). Patients of group "BC" were administered 3 ml (15 mg) of hyperbaric bupivacaine (0.5%) + 30mcg (0.2 ml) of clonidine + 0.3 ml normal saline. After spinal anaesthesia, Oxygen (4L/min) by facemask was given.

Sensory block was assessed by pin pricks in mid clavicular line bilaterally using 27 guage hypodermic needle. The onset of sensory block was considered as the time from injection of the drug into the sub arachnid space to the attaining of sensory block to T10 level[15]. The duration of sensory block was taken from the time of intrathecal injection of drug to regression of the level of sensory block to L1 dermatome[18]. Sensory block assessment was made every 60 seconds for first 10 minutes and then every 15 minutes till the block regress to LI dermatome.

- Motor block was assessed using modified bromage scale. Time interval between injection of drug into subarachnoid space, to the patient's inability to lift the straight extended leg was taken as onset time. Duration of motor block was recorded from onset time to time when the patient was able to lift the extended leg. Motor block was assessed every 60 sec for first 10 minutes and then every 15 minutes till the patient was able to lift the extended leg.

Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure, Respiratory Rate and $Sp0_2$ were monitored at 0, 5, 10, 15, 20, 25, 30, 40, 50, 60, 75, 90, 150, 210 minutes. The incidence of hypotension[32] (systolic arterial blood pressure < 20 % of baseline), was treated with intravenous fluids and if the fall was more than 30%of the baseline fluid administration was supported by Inj.Ephedrine 6 mgintravenous boluses titrated to effect.Bradycardia defined as any fall in the heart rate < 50/ min and was treated by atropine 0.6 mg intravenous.

- Side effects like sedation, nausea, vomiting, pruritus was monitored in intraoperative and post operative period till the administration of rescue analgesic. Sedation scores were assessed every 15 minutes intra operatively, every hourly post operatively till administration of rescue analgesic using a four-point score described by Chernik et al [6].

STATISTICAL ANALYSIS

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuum measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two groups. The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

Number of male and female patients in the both the groups which was comparable and there was no statistically significant difference between two groups .Number of ASA grade I and II patients in the both groups 15 each were comparable.

Table-1: - Comparison of demographic parameters between the groups

	Group	Mean	SD	Mean difference (95% CI)	T	df	p-value
Age	**BF**	41.10	10.30	0.53(-4.22,5.29)	0.22	58	0.82(NS)
	BC	40.57	7.95				
Weight	**BF**	57.00	6.02	0.13 (-2.70, 2.96)	0.09	58	0.93(NS)
	BC	56.87	4.87				
Height	**BF**	167.23	4.69	1.00(-147,3.47)	0.81	58	0.42(NS)
	BC	166.23	4.89				

The above table shows the mean age, weight and height of the patients in group BF and group BC. There was no statistically significant difference between the two groups, P value .182

Table-2: - The Type of Surgical procedure

Surgery	Group		Total
	BF	BC	
Lower Limb Surgery	15(50.0%)	15(50.0%)	30
Urological Surgery	15(50.0%)	15(50.0%)	30
Total	30	30	60
Chi square test	Chi square value (1) = 0.00, p = 1.00 (NS)		

There is no statistical difference between type of surgery in present study

Table-3: - Comparisons of onset and duration of sensory and motor block between the study groups

sensory block	Group	N	Mean	SD	Mean Difference (95% CI)	t	df	p-value
Onset	**BF**	30	298.00	36.90	-18.00(-37.46, 1.46)	-1.85	58	0.07(NS)
	BC	30	316.00	38.38				
Duration	**BF**	30	177.50	12.51	-27.00(-33.53, -20.47)	-8.28	58	< 0.001*
	BC	30	204.50	12.75				
Motor block								
Onset	**BF**	30	348.00	36.62	-18.00(-42.34, 6.34)	-1.49	50.29	0.14(NS)
	BC	30	366.00	55.37				
Duration	**BF**	30	238.00	12.29	-29.50(-36.82, -22.19)	-8.07	58	< 0.001*
	BC	30	267.50	15.80				

From the above tables and graphs, it is evident that there was no statistically significant difference between two groups with respect to the time of onset of sensory and motor block. The duration of sensory and motor block was more in clonidine group as compared to fentanyl group which was statistically significant.

Table-4: - Comparison of duration of complete and effective analgesia between the study groups

	Group	N	Mean	SD	Mean Difference (95% CI)	t	df	p-value
Onset	**BF**	30	282.00	12.08	-73.50(-80.63, 66.37)	-20.63	58	<0.001*
	BC	30	355.50	15.33				
Duration	**BF**	30	292.00	13.49	-72.00(-79.57, -64.43)	-19.03	58	< 0.001*
	BC	30	364.00	15.72				

The mean duration of complete analgesia in group BF was 282 min and in group BC was 355.5 min. Statistically significant difference was observed between the two groups with respect to the duration of complete analgesia as significance value obtained from independent sample's t test was less than 0.05 (p= 0.001).

The mean duration of effective analgesia in group BF was 292 min and in group BC mean duration of effective analgesia was 364 min. Statistically significant difference was observed between the two groups with respect to the duration of effective analgesia as significance value obtained from independent sample's t test was less than 0.05 (p= 0.001).

Statistically there were no significant changes in the Systolic blood pressure, diastolic blood pressure, heart rate, oxygen saturation, between the study groups at different time intervals with significant values more than 0.05.

Table-5: Distribution of Side Effects

		Group		Total	Fishers exact test
		BF	**BC**		**p-value**
Bradycardia	**No**	**26(86.7%)**	**25(83.3%)**	**51(85.0%)**	**1.00(NS)**
	Yes	**4(13.3%)**	**5(16.7%)**	**9(15.0%)**	
Hypotension	**No**	26(86.7%)	25(83.3%)	51(85.0%)	1.00(NS)
	Yes	4(13.3%)	5(16.7%)	9(15.0%)	
Nausea	**No**	29(96.7%)	28(93.3%)	57(95.0%)	1.00(NS)
	Yes	1(3.3%)	2(6.7%)	3(5.0%)	
vomiting	**No**	30(100.0%)	30(100.0%)	60(100.0%)	-1.00
Pruritus	**No**	27(90.0%)	30(100%)	57(95.0%)	0.24(NS)
	Yes	3(10.0%)	0(0%)	3(5.0%)	

There were no significant differences between the two groups with respect to the occurrence of Bradycardia, hypotension, nausea, vomiting and pruritis

Table-6: - Distribution of the study participants according to the sedation score among the study groups

Sedation score	Group		Total
	BF	BC	
0	25(83.3%)	23(76.7%)	48(80.0%)
1	5(16.7%)	7(23.3%)	12(20.0%)
Chi square test: Chi square value(1)= 0.42, p= 0.2(NS)			

Significance value from Chi square test is 0.2. Majority of people in both groups did not have any significant sedation. There were no statistical differences in the sedation scores between the two groups.

DISCUSSION

Subarachnoid block with bupivacaine has been most extensively used for lower abdominal and lower limb surgeries because of its simplicity, speed, reliability and minimal exposure to depressant drugs. However, a single intrathecal injection of bupivacaine provides analgesia for only 2 to 2.5 hours. Most patients require further analgesia during post operative period. Various adjuvants to intrathecal local anaesthetics such as opioids, ketamine, alpha 2 agonists, neostigmine are often added to enhance the duration and quality of spinal anesthesia, however each drug has its own limitations. Neuraxial administration of opioids and alpha 2 agonists along with local anaesthetics improves quality of intra operative analgesia and also provides post operative pain relief for longer duration.

An attempt has been made in this study to compare low dose of Clonidine (30 micrograms) with Fentanyl(25 micrograms) as adjuvant to intrathecal bupivacaine to find out which is better adjuvant. This clinical study is a randomized, prospective, double-blind study, was done in 60 patients, who were randomly allocated into two groups namely group BF and BC. Patients belonging to group BF received 3 ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.5 ml (25 microgram) fentanyl. Patients of group BC received 3 ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.2 ml (30 microgram) clonidine + 0.3 ml of normal saline. In our study the patients studied across the group did not vary much with respect to age, sex, ASA grades, weight, height and type of surgery.

In the present study the onset of sensory blockade was considered as the time from injection of the drug into the subarachnoid space to the attaining of sensory block to TIO level. The onset of sensory block in fentanyl group was 298 +36.90 sec and in clonidine group 316 ± 38.38sec. There was no statistically significant differencebetween the two groups with respect to the onset of block, as significance value obtained from independent sample's t test was more than 0.05 (p= 0.07). Similar values were obtained with regard to the onset of sensory block in clonidine group in a study conducted by K.P. Polaiah et al.[7], in 2015 (4.2.0.02min) when 30 ug of clonidine was used as adjuvant to 3 ml of 0.5% hyperbaric bupivacaine and similar values were obtained in fentanyl group in a study conducted by Dr. Amit A Chandak et al.,[8] in 2013(4.75.0.6 min) when 25ug of fentanyl was used as adjuvant to 3 ml of 0.5% hyperbaric bupivacaine. Vidhi Mahendre et al.[9], in 2013 and Hina Bashirn et al.,[10] in 2015 found that there was no statistically significant difference observed (p>0.05) with respect to onset of sensory blockade, when 25 ug fentanyl and 30 ug clonidine compared as adjuvants to intrathecal hyperbaric bupivacaine. Our finding is in accordance with their study. Duration of sensory blockade: The duration of sensory block was considered from the time of injection of drug to regression of the level of sensory block to LI dermatome. The mean duration of sensory block in group BF was 177.50.12.51 min and in group BC it was 204.50.12.75min. Statistically significant difference was observed between the two groups

with respect to the duration of sensory block as significance value obtained from independent sample's t test was less than 0.05 (p< 0.001). Kumkum Gupta' et al[11]., in 2016 studied effects of 25 ug fentanyl and 30 ug clonidine as adjuvants to 3.5m1 of 0.5% hyperbaric bupivacaine and found that duration of sensory block(mean time of two segment regression) was more in clonidine group(121.33.14.31min) when compared to fentanyl group(102.33.05 min) which was statistically significant (p=0.005). GurpreetSingh et al.[12], in 2016 studied the effects of 25 ug fentanyl and 30 ug clonidine as adjuvants to 2m1 of 0.5% hyperbaric bupivacaine and found that duration of sensory block(time of regression of block from highest sensory block to T12 level) was more in clonidine group(155.17 ±17.49 min) as compared to fentanyl group(135.33 ±12.59 min) which was statistically significant (p<0.05). Radhe Shame et al.[13], in 2016 compared the effects of intrathecal clonidine 30 micrograms and fentanyl 25 micrograms as additives to intrathecal ropivacaine 18.75 mg. They found out that statistically significant difference (p=0.001) was observed in the duration of sensory blockade(time for regression of block to L5 dermatome) with clonidine(240±20.99min) and fentanyl (196.80±18.34min). Our study finding is in accordance with above studies.

In the present study the onset of motor blockade was taken as the time interval between injection of drug into subarachnoid space, to the patient's inability to lift the straight extended leg. The onset of motor block in fentanyl group was (348 ±36.62sec) and in clonidine group it was (366.00±55.37 sec). There was no statistically significant difference between the two groups with respect to the onset of motor block, as significance value obtained from independent sample's t test was more than 0.05 (p= 0.14). Similar values were obtained, with regard to the onset of motor block in clonidine group in the study conducted by K.P. Polaiah[7] et al., in 2015 (5.573±0.0464 min) when 30ug of intrathecal clonidine was used as adjuvant to 3m1 of 0.5% hyperbaric bupivacaine and similar values were obtained in fentanyl group in the study conducted by Anita Chhabra R[18] et al., in 2013 (6.02±2 min) when 25ug of fentanyl was used as adjuvant to 3 ml of 0.5% hyperbaric bupivacaine. Vidhi Mahendru[9] et al., in 2013 and Hina Bashir et al.[10], in 2015 found that there was no statistically significant difference observed (p>0.05) with respect to onset of motor blocked, when 25 ug fentanyl and 30 ug clonidine compared as adjuvants to intrathecal 0.5% hyperbaric bupivacaine. Our finding is in accordance with their study.

The duration of motor block will be considered from the onset time to time when the patient was able to lift the extended leg. The mean duration of motor block in group BF was 238.00±112.29 min and in group BC, it was 267.50±115.80 min. Statistically significant difference was observed between the two groups with respect to the duration of motor block as significance value obtained from independent sample's t test was less than 0.05 (p.<0.001). Kumkum Gupta et al[11], in 2016 studied effects of 25 ug fentanyl and 30 ug clonidine as adjuvants to 3.5m1 of 0.5% hyperbaric bupivacaine and found that duration of motor block was more in clonidine group(242.53±129.32min) when compared to fentanyl group(188.501±40.06 min) which was statistically significant. (p=0.000). Radhe Sharan et al.[13], in 2016 compared the effects of intrathecal clonidine 30 micrograms and fentanyl 25 micrograms as additives to intrathecal ropivacaine 18.75mg and found that statistically significant difference (p=0.001) was observed in the duration of motor blockade with clonidine(192.20±17.36min) and fentanyl (139.20±117.93min). Our study finding is in accordance with above studies.

Duration of complete analgesia was taken as from the time of intrathecal drug administration to the first report of pain. The mean duration of complete analgesia in group BF was 282.001±12.08 min and in group BC mean duration of complete analgesia was 355.50±115.33 min. Statistically significant difference was observed between the two groups with respect to the duration of complete analgesia as significance value obtained from independent sample's t test was less than 0.05 (p<0.001). Duration of effective analgesia was

taken as from the time of intrathecal drug administration to the time of first supplementation with rescue analgesic. The mean duration of effective analgesia in group BF was 292.00±113.49 min and in group BC, mean duration of effective analgesia was 364.00±115.72 min. Statistically significant difference was observed between the two groups with respect to the duration of effective analgesia as significance value obtained from independent sample's t test was less than 0.05 ($p<0.001$). Kumkum Gupta et al.[11], in 2016 studied effects of 25 ug fentanyl and 30 ug clonidine as adjuvants to 3.5m1 of 0.5% hyperbaric bupivacaine and fond that the duration of analgesia was more in clonidine group(283.00±140.18min) when compared to fentanyl group (231.50±46.18min) which was statistically significant. (p.1000). Radhe Sharan et al.[13], in 2016 compared the effects of intrathecal clonidine 30 micrograms and fentanyl 25 micrograms as additives to intrathecal ropivacaine 18.75 mg and found that statistically significant difference ($p=0.001$) was observed in the duration of effective analgesia between clonidine (408.00±141.99min) and fentanyl (295.20±131.20min) . Our study finding is in accordance with above studies.

Hemodynamic parameters were comparable at different time intervals in the BF and BC groups. There was no statistically significant difference in the heart rate, systolic and diastolic blood pressure at different time intervals in the BF and BC groups ($p> 0.05$). There was no statistically significant difference between the two groups with respect to the occurrence of bradycardia ($p=1.0$) and hypotension ($p=1.0$) as the significance values obtained were more than 0.05 for each of these variables. 13.3% of people in group BF and 16.7% of people in group BC developed bradycardia Majority of people in both the groups (86.7 % in group BF and 83.3 % in group BC) did not develop bradycardia. 13.3 % of people in group BF and 16.7 % of people in group BC developed hypotension. Majority of people in both groups (86.7 % in group BF and 83.3 % in group BC) did not develop hypotension.

Khanna MS et al.[14], in 2002 found that using fentanyl 25 microgram intrathecally as adjuvant to spinal bupivacaine, does not cause statistically significant hypotension or bradycardia. Sukhminder Jit Singh Bajwa, et al.[15] in 2012 found that using clonidine30 microgram intrathecally as adjuvant to spinal bupivacaine, has no association with significant hypotension or bradycardia. Vidhi Mahendru et al.[9] in 2013, Hina Bashir et al[10]., in 2015 and Kumkum Gupta et al.[11], in 2016 compared 25ug fentanyl and 30 ug clonidine as adjuvants to spinal bupivacaine and found that there was no statistically significant difference between the two groups regarding occurrence of hypotension or bradycardia. Our study findings are in accordance with the above studies.

There was no statistically significant difference in the mean respiratory rates, SPO_2 at different time intervals in the BF and BC groups ($p> 0.05$). In both groups at any time interval, there was no occurrence of respiratory depression (spo2<90% and Respiratory rate<8/min). Hadil Magdi Abdel H[16] in 2009, Vidhi Mahendru et al.[9], in 2013, and Hina Bashir et al[10]., in 2015 also found thatusing fentanyl 25ug or clonidine 30 microgram intrathecally as adjuvant to spinal bupivacaine does not cause respiratory depression.

There were no statistically significant differences between the two groups with respect to the occurrence of nausea as the significance value ($p=1.00$) obtained from Fisher's exact test was more than 0.05. Nausea was seen in 3.3% of people in fentanyl group and 6.7% in clonidine group. Sukhminder Jit Singh Bajwa, et al.[15] in 2012 found that using clonidine 30 micrograms has caused less nausea and vomiting when compared to bupivacaine alone. Vidhi Mahendre et al,[9] in 2013, HinaBashirnet al.,[10] in 2015 found that fentanyl 25ug and clonidine 30ug as intrathecal adjuvants to hyperbaric bupivacaine were comparable in the occurrence of nausea. Our study is in accordance with above studies.

In our study none of the patients developed vomiting. Similarly in a study conducted by Kumkum Gupta et al.[14], in 2016 none developed vomiting when they compared fentanyl 25ug and clonidine 30ug as adjuvants to spinal bupivacaine.

In fentanyl group 10% of people developed pruritus whereas none in clonidine group. The association of pruritus with fentanyl was statistically not significant as the significance value (p=0.24) from Fisher's exact test was more than 0.05. In a study done by Vidhi Mahendru et al.[9] in 2013, pruritus was found in fentanyl group but it was notsignificant statistically(p=0.1), which is in accordance with our study.

In our study, we found that there was no statistically significant difference in sedation scores between BF and BCgroup (p=0.2). H Saxena et al.[17], in 2009 and Shah Bhavini B et al.[18], in 2012 found that using low dose (clonidine 30 microgram) intrathecally does not cause significant sedation. Vidhi Mahendre et al[9]., in 2013 and Kurnkum Guptaet al.[11], in 2016 found that 25 ug of fentanyl and 30ug clonidine are comparable in sedation scores when used as adjuvants to intrathecal bupivacaine which is in accordance with our study.

Our findings corroborate with the findings of studies conducted by Kumkum Gupta et al.[11], in 2016 who compared clonidine 30 micrograms, fentanyl 25 micrograms as additives to intrathecal hyperbaric bupivacaine 17.5mg and Radhe Sharan et al.[13], in 2016, who compared the effects of clonidine 30 micrograms, fentanyl 25 micrograms as additives to intrathecal ropivacaine 18.5 mg.

The following table compares our study finding with the other two studies.

Table-7: Comparison with other simile,

Difference between clonidine and fentanyl group	Our study	Study by Radhe Sharan, et al.[13]	Study by Kumkum Gupta, et al.[11]
Onset of sensory block	Not significant	Not significant	Significant
Duration of sensory block	significant	significant	Significant
Onset of motor block	Not significant	Not significant	Significant
Duration of motor block	significant	significant	Significant
Duration of analgesia	significant	significant	Significant
Hemodynamic parameters	Comparable	Comparable	Comparable
Side effects	Not significant	Pruritus was more in Fentanyl group	Not significant

Hence in our study, we found that intrathecal combination of bupivacaine and clonidine offers advantages In terms of sensory, motor block, complete and effective analgesia as compared to fentanyl. Hemodynamic parameters are comparable and side effects are not significant in both the groups.

CONCLUSION

The present study concludes that Statistically significant difference was not observed in the onset of sensory, and motor blockade when fentanyl 25 microgram or clonidine 30 microgram was used as additive to intrathecal hyperbaric bupivacaine for spinal anaesthesia. Compared to fentanyl 25 microgram, clonidine 30 microgram as additive to intrathecal hyperbaric bupivacaine for spinal anaesthesia, prolonged the duration of sensory and motor blockade which was statistically significant. Compared to fentanyl 25 microgram, clonidine 30 microgram as additive to intrathecal hyperbaric bupivacaine for spinal anaesthesia, prolonged the duration of complete and effective analgesia,which was statistically significant Statistically significant difference was not observed in hemodynamic parameters between clonidine and fentanyl group. There were no significant side effects, observed in both the groups.

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