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ORIGINAL RESEARCH

Comparison of Intrathecal Nalbuphine and Fentanyl as an Adjuvant to Bupivacaine in Spinal Anaesthesia for Elective Caesarean Section: A Randomized Clinical Study

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ABSTRACT

Background: Spinal anaesthesia is the preferred anaesthetic technique for Caesarean section as it has rapid onset of action. Bupivacaine is an amide local anaesthetic which is most used drug in spinal anaesthesia. It has slower onset of action, high potency, and a relatively short postoperative analgesia. The quality and duration of sensory blockage are enhanced when adjuvants are added to intrathecal local anaesthetics. Many studies have compared the effect of intrathecal nalbuphine & fentanyl with Bupivacaine in lower abdominal and lower limb orthopaedic surgeries. **Methods:** This is a Prospective Randomized Double blinded study conducted in Institute of Obstetrics and Gynaecology, Chennai in 2021. This includes 60 female patients who were 20-40 yrs old, Full-term Singleton Parturient, patients were randomly allocated into two groups - Group A and Group B with 30 parturient each, Group A patients received Bupivacaine and Nalbuphine and Group B received Bupivacaine and Fentanyl. **Result:** Age, BMI (kg/m2) and duration of surgery were compared among the Groups by Unpaired t-test showed no statistically significant difference. But onset of sensory blockade, time taken for maximum sensory blockade, Onset of motor blockade, Two segment Regression time, duration of complete and effective analgesia were compared among the two groups which showed statistically significant difference. **Conclusion:** Intrathecal Fentanyl as an adjuvant to 0.5% Hyperbaric Bupivacaine was superior to Nalbuphine in the onset of both sensory and motor blockade. Nalbuphine is superior to Fentanyl for increasing the duration of postoperative analgesia and reduced requirement of rescue analgesia and reduced incidence of postoperative shivering.

Key words: Spinal anaesthesia, 0.5% Bupivacaine, Nalbuphine, Intrathecal opiods.

INTRODUCTION

Spinal anaesthesia is the preferred anaesthetic technique for Caesarean section as it has rapid onset of action and it is simple to perform. It also reduces the risk of maternal pulmonary aspiration, reduces the risk of neonatal exposure to depressant drugs. Bupivacaine is an amide local anaesthetic which is commonly used in spinal anaesthesia. It has slower onset of action, high potency, and a relatively short postoperative analgesia. During caesarean delivery, patient may experience visceral pain due to peritoneal traction and handling of intraperitoneal organs. Occurrence of intra operative visceral pain can be reduced by increasing the dose of intrathecal local anaesthetic but at the expense of a higher blockade.

Advantages of adding adjuvants to intrathecal local anaesthetics are that they improve the quality and duration of sensory blockade. Intrathecal opioids have synergistic action with local anaesthetics. They produce intense sensory block without causing increase in sympathetic block. They reduce the dose of local anaesthetic required. They can provide better

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hemodynamic stability. They are associated with less side effects. Fentanyl is a highly selective mu opioid receptor agonist. It is lipophilic and has rapid onset of action after intrathecal administration. It prolongs the duration of sensory blockade. It also prolongs the duration of post operative analgesia without producing much complications. Nalbuphine is a mixed synthetic kappa agonist and mu antagonist. It enhances kappa opioid effects thereby producing analgesia and attenuates mu opioid effects thereby producing fewer side effects. Nalbuphine prolongs the duration of post operative analgesia when used as an adjuvant to intrathecal local anaesthetics. Many studies have compared the effect of intrathecal nalbuphine & fentanylwith Bupivacaine in lower abdominal and lower limb orthopaedic surgeries.

The aim of the present study is to compare the post operative analgesic efficacy of intrathecal fentanyl and nalbuphine as an adjuvant to Bupivacaine in patients undergoing Elective Lower Segment Caesarean Section.

MATERIALS AND METHODS

The study was conducted after obtaining the Institutional Ethical Committee approval. Study design: This is a Prospective Randomized Double blinded study.

Sample size calculation: This study included 60 female patients who were classified under American Society of Anaesthesiologists Physical Status 1 or 2 planned for Elective Lower Segment Caesarean Section. According to Farahat et al study, considering the mean and standard deviation of duration of effective post op analgesia in Nalbuphine group as 225.4 ± 82.3, mean and standard deviation of duration of effective post op analgesia in Fentanyl group as 176.1 ± 46.4 at 95% confidence interval with 80% power, the sample size is calculated as 30 for each group and the total sample size is 60.

Inclusion Criteria: 20-40 yrs old Full-term Singleton Parturient American Society of Anaesthesiologists Physical Status 1 and 2 Elective Caesarean Section Patient who gave valid informed consent for the study.

Exclusion Criteria: Patients posted for Emergency Caesarean section Complicated Pregnancy, Intrauterine fetal compromise, Morbid obesity, Patients with Cardiovascular, Neurological, Hepatic or Renal disease, Contraindication to Subarachnoid block like patient refusal, Coagulopathy, Allergy to Local Anaesthetic drugs, Local infection at injection site.

Study centre and study period: Institute of Obstetrics and Gynaecology, Madras medical college, Chennai. Duration of study is from January 2021-June 2021.

Preoperative assessment: The preoperative assessment chart was checked. History of any comorbid illness, previous surgery and Anaesthesia were documented. Physical examination was done. General condition of the patient, Height, Weight and BMI, Vital signs were noted. Examination of CVS, RS, CNS, Abdomen were done. Airway examination and Spine examination were done. Preoperative investigations were done which included CBC, Bleeding time, Clotting time, Blood sugar, Renal Function Test and ECG. Patients who met inclusion criteria were educated about the Visual analogue scale score (VAS) which was used to assess postoperative pain score.

Consent: Patients were explained about the clinical study, anaesthetic technique, drugs used in the study and its complications. Informed and written consent obtained.

Premedication: Patients were advised NPO for 8 hours before surgery. The patients were premedicated with Inj. Metoclopramide 10 mg IV and Inj. Ranitidine 150 mg IV 45 minutes prior to surgery. Preparation: After shifting the patients to OT in left lateral position standard monitors like Electrocardiography (ECG), Non-Invasive Blood Pressure(NIBP) and Pulseoximetry were connected. Baseline reading of Blood pressure, Oxygen saturation (SpO2), Pulse rate and Respiratory Rate were recorded. Patients were cannulated with 18G venflon in upper limb to secure IV line. Preloading was done with 10ml//kg Crystalloid solution (Ringer lactate) over 15 minutes. Patients were randomly allocated into two groups - Group A and Group B with 30 parturient each, using computer generated randomized numbers and sealed opaque envelop technique.

Materials

Drugs

- Inj Bupivacaine 0.5% Hyperbaric solution
- Inj.Nalbuphine hydrochloride
- Inj. Fentanyl Citrate
- Emergency drugs

Equipment's

- Sponge holding forceps
- Sterile drapes and sterile bowl
- Sterile gauze pieces
- Sterile 2ml and 5ml syringes
- Spinal Needle: 25G Quincke Babcock needle

Technique: Under strict aseptic precaution with patient in sitting position and leaning forward, parts were painted and draped. Using midline approach, L3-L4 intervertebral space was identified and infiltrated with 2ml of 2% Lignocaine. Subarachnoid block was performed with 25G Quincke-Babcock needle. After obtaining clear free flow of Cerebrospinal fluid, the drug was injected at the rate of 0.2ml/sec.

GROUP A patients received 10mg (2ml) of 0.5% Bupivacaine and Nalbuphine 800mcg(0.5ml)-Total volume of drug is 2.5ml.

GROUP B patients received 10(2ml) of 0.5% Bupivacaine and Fentanyl 25mcg(0.5ml)-Total volume of the drug is 2.5ml

Patient was immediately placed in supine position. Supplemental oxygen was administered via face mask

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at 6L/min. A wedge was kept under right gluteal region. Patient's hemodynamic parameters like Heart rate, Pulse rate, Non-Invasive Blood Pressure and Respiratory rate were monitored and recorded during procedure and at 5 ,10,15,20,25, and 30 minutes after subarachnoid block, and subsequently every 15 minutes up to 1 hour and postoperatively upto 6hrs

Sensory Block: It was assessed by loss of pin-prick sensation in the midclavicular line with 27G needle, every minute until block reached T6 dermatomal level. After that, it was checked every 2 minutes until maximum level of sensory block was achieved. Then it was checked every 5 minutes for the next 20 minutes and then every 15 minutes until two-segment regression from maximum dermatomal block. Onset of sensory block is the time required to achieve loss of pin-prick sensation at T6. Maximum level of sensory block and time required to achieve maximum level of sensory block was noted Surgery was proceeded once sensory block reached T6 level. Time interval between injection of local anaesthetic drug to two-segment regression from maximum dermatomal block was noted. Motor Block:It was assessed using modified Bromage scale. Onset of complete motor blockade -it is the time interval between injection of local anaesthetic drug to grade 3 Bromage scale. Duration of Motor Blockade: Time interval between injection of Local anaesthetic drug to return of motor blockade to Bromage Grade 1

Quality of Surgical Anaesthesia

Excellent: No complaint of pain during surgery

Good: Complains of minimal pain or discomfort which is treated with Inj.Pentazocine 0.5mg/kg IV

Poor: Requires administration of General Anaesthesia

Post-Operative:

Postoperatively patients were monitored for heart rate, non-invasive blood pressure, Respiratory rate, and oxygen saturation. Postoperatively pain assessment was done using Visual Analog Scale. VAS score was assessed hourly for the first 4 hours, then at 12 hr and 24 hr. Duration of complete analgesia: Time interval between Injection of local anaesthetic drug to first sensation of pain (VAS Score >0) was noted. Duration of Effective Analgesia: Time interval between injection of local anaesthetic drug and the requirement of first analgesic intervention(VAS Score > 3) where Inj. Tramadol 50mg IM was given as rescue analgesic. Number of rescue analgesics required in a 24 hourperiod postoperatively was recorded. Patients were monitored for side effects like nausea, vomiting, hypotension, bradycardia, pruritus, shivering and sedation.

Neonatal outcome: Assessment of neonate was done using APGAR score at 1 and 5 mins

Statistical Analysis: The collected data were analyzed with IBM.SPSS statistics software 28.0 Version.

RESULT

60 patients participated in the study.Table-1 shows comparison between age groups by Pearson's chi-squared test X2=0.219, p=0.97>0.05 which shows no statistically significant association between Age and Groups and were comparable. Table-2 shows comparison of BMI (kg/m2) and duration of surgery among the Groups by Unpaired t-test showed that there is no statistically significant difference between the Groups.

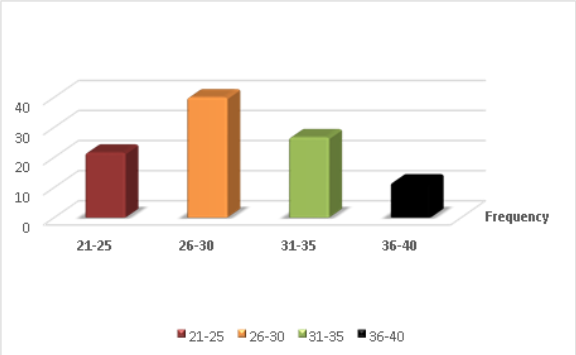

Fig-1 Age distribution

Table-1 Comparison of Age between Groups

Age (years)	Group		Total	Chi Square X^2	P-Value
	Group-A N=30	Group-B N=30	N=60	0.219	0.974
21–25	6	7	13		
26-30	12	12	24		
31-35	8	8	16		
36-40	4	3	7		
	P>0.05, Hence not significant				

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Table-2 Comparison of various parameters among Groups

Parameter	Mean/SD	Group-A 0.5% Bupivacaine and Nalbuphine	Group- B 0.5% Bupivacaine and Fentanyl	Unpaired T-test	P value
BMI	Mean age (years)	25.88	27.75	1.576	0.12
	SD	3.73	5.32		
Durationof surgery	Mean(minutes)	55.50	53.67	0.812	0.41
	SD	8.84	8.60		
Onset of Sensory blockade(seconds)	Mean(seconds)	292	256	2.821	**0.0065* HS**
	SD	53.97	44.38		
Time for maximum sensory Blockade	Mean(seconds)	348	310.60	2.89	**0.0054* HS**
	SD	44.13	55.44		
Onset of Motor blockade	Mean(minutes)	5.67	5.10	3.007	**0.0039* HS**
	SD	0.84	0.61		
Duration of Motor blockade(minutes)	Mean(minutes)	154.67	152	1.88	0.09
	SD	5.56	6.64		
Two segment Regression time	Mean(minutes)	115.33	103.0	5.497	**0.0001* HS**
	SD	7.98	9.34		
Duration of Complete Analgesia (minutes)	Mean(minutes)	181.17	137.50	8.789	**0.0001* HS**
	SD	23.59	13.57		
Duration of Effective Analgesia (minutes)	Mean(minutes)	248.83	207.33	8.47	**0.0001* HS**
	SD	21.96	14.84		
	SD	0.57	0.76		

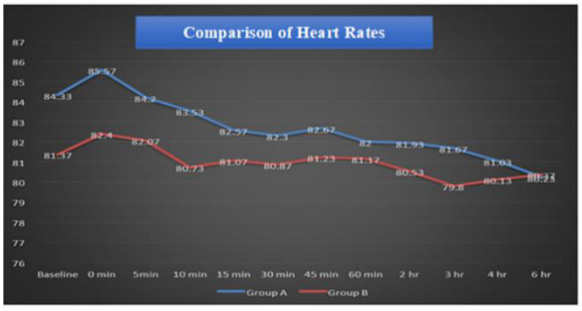

Fig-2 Comparison of Heart rates

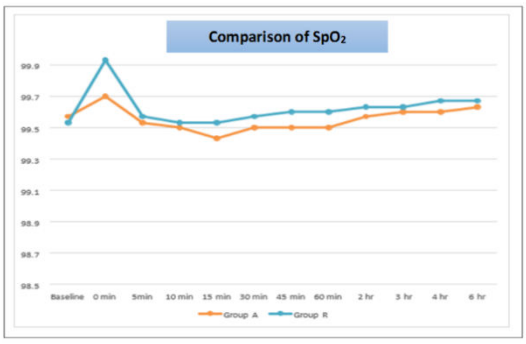

Fig-3- Comparison of SpO2

Heart rate, SpO2, Respiratory rates were compared among the Groups by Unpaired t-test. This is demonstrated in Fig-2, Fig-3, and Fig-4 respectively. Though the heart rates were relatively lower in Group B, p-value was >0.05, is not a statistically significant difference and therefore they are not comparable. No statistically significant difference in SpO2 and respiratory rates between the Groups were present. Fig -5 shows Mean Arterial Pressure with Groups by Unpaired t-test: all the time durations comparisons show p>0.05, which is not a statistically significant difference in the Mean Arterial Pressure between the Groups.

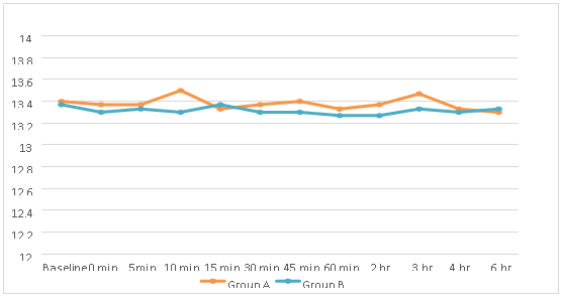

Fig-4 Comparison of Respiratory Rates among groups

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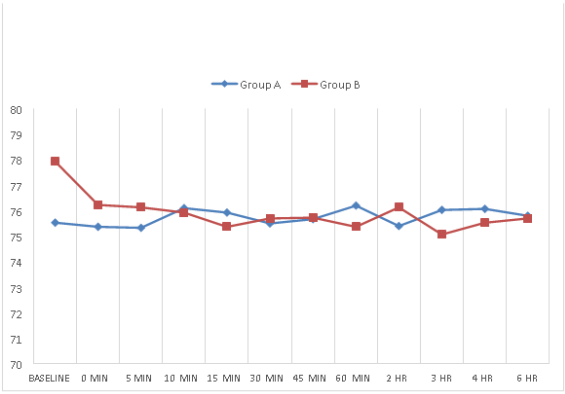

Fig-5 Comparison of Mean Arterial Pressures

Onset of sensory blockade, time taken for maximum sensory blockade, Onset of motor blockade, two segment Regression time, duration of complete and effective analgesia were compared among the two groups. Table-2 shows that there is highly significant difference among the groups in all these values. The height of sensory dermatome blocked after subarachnoid block were compared in both the study groups following intrathecal Nalbuphine and Fentanyl which is shown in Table-3. A majority of 70% of the parturient achieved a T4 dermatome following intrathecal Nalbuphine, while 50% achieved T3 following intrathecal Fentanyl. The sensory dermatomal levels in my study were T3 to T6. These were statistically compared using Chi square test. The X2 value was 11.31 and p=0.01. The quality of surgical anaesthesia was graded as excellent, if no complaints of pain at any time during surgery, Good, if there is minimal pain or discomfort and Poor, if regional technique has to be converted into general anaesthesia. In this current study, the quality of analgesia was comparable between intrathecal Nalbuphine and Fentanyl when compared with Chi-square test, with a p value 0.30 shown in Fig-6.

Table- 3 Comparison of Maximum height of dermatomal block

MAXIMUM HEIGHT OF DERMATOMAL BLOCK	GROUP A N=30		GROUP B N=30		Chi Square Test	P value
T3	4	13.3%	15	50%	11.31	0.01
T4	21	70%	9	30%		
T5	3	10%	4	13.3%		
T6	2	6.7%	2	6.7%		
P<0.05, hence significant						

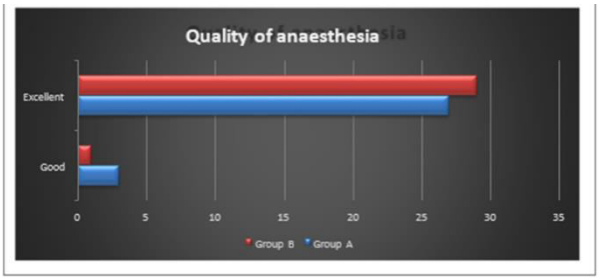

Fig-6 Quality of Anaesthesia

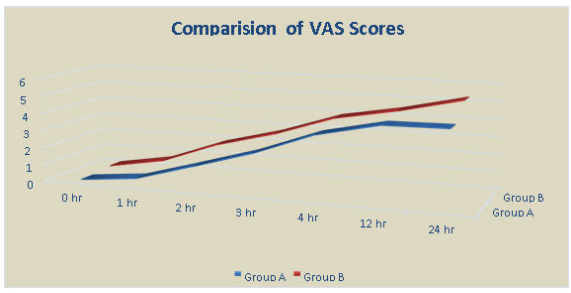

Fig- 7 Comparison of VAS Scores

The above Fig-7 shows comparison of Visual Analog Scale score within Groups by Unpaired t-test. There were significant differences in the mean VAS scores up to 4 hours and no significance in the 12th and 24th hours. Patients in Group A had lower VAS scores than those in Group B. The Fig-8 shows comparison of neonatal APGAR score within Groups by Unpaired t-test: There were no significant differences in the mean APGAR scores at both 1st and 5th minute after birth.

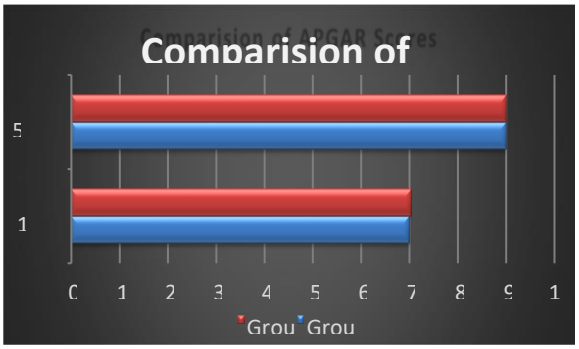

Fig-8 Comparison of APGAR Scores

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Table- 4 Number of Rescue analgesics and Comparison of Ramsay Sedation Scores

Parameter	Mean/SD	Group-A	Group-B	Unpaired T-test	P value
Number of Rescue Analgesics	Mean	1.87	2.33	**2.652**	**0.01* S**
	SD	0.57	0.76		
Ramsay Sedation Scores	Mean	2.17	2.07	**1.204**	**0.23**
	SD	0.38	0.25		

Post-Op Complications at 0 Hr

In Nalbuphine group, 3 patients had hypotension and in Fentanyl group, 4 patients had hypotension and its p value is 0.72 which is not statistically significant. The hypotension was managed with crystalloids and Inj. Ephedrine 6 mg IV dose. Similarly, in Nalbuphine group, 2 patients had vomiting as side effect but in Fentanyl group., three patients had vomiting. It has no statistical significance with p value 0.65. The nausea and vomiting were managed with crystalloids and Inj. Ondansetron 8mg IV. In Nalbuphine group, no patients had pruritis, while two in Fentanyl group developed pruritis. But it was also not statistically significant with p=0.13.However, Shivering was more pronounced in Fentanyl (16.7%) than Nalbuphine group (3.33%), which was statistically significant.

DISCUSSION

Both intervention groups were similar with respect to the age distribution, BMI distribution, ASA Physical status.All the parturient enrolled in this study belonged to ASA Physical Status II (n=60). There were no statistical differences between the two groups in the above mentioned parameters. This was in concordance with other studies like Farahatet al, and Bindra TK et al[1],[2]. The mean duration of surgery was similar to the study done by Hala Mostafa Gomaa et al[3]. It was observed that there was no statistically significant difference between both the intervention groups in relation to the Mean arterial blood pressures similar to the study done by Gupta K et al and Prabhakaraiah et al[4][5]. Intrathecal Fentanyl as an adjuvant helps in the early onset of sensory blockade when compared to Nalbuphine. Similar results were seen in the studies done by Rashmi Bengali et al[6]. The height of sensory dermatomal levels after subarachnoid block were compared among groups which showed statistically significant difference. The time for regression of the sensory blockade by two segments was shorter in Fentanyl Group (103±9.34mins) than Nalbuphine(115.33±7.98mins). this implies that the patients in Nalbuphine group retained the sensory blockade at the highest dermatomal level for a longer period than those in Fentanyl similar to study done by Sharma et al[7]. The patients in Nalbuphine group experienced complete and effective analgesia for a longer duration than those of Fentanyl group. Mean VAS scores were significantly lower in the Nalbuphine group when measured at hourly intervals for the first 4 hours. However, in the 12th and 24th hours scores, both the groups were comparable in terms of VAS Scores (p value of 0.23 and 0.20 respectively). This was similar to the studies conducted by Bindra TK et al[2].The number of rescue analgesics were compared in both the groups which was statistically significant with p value of 0.01. When the sedation scores among the groups was compared, it was not statistically different. But Naaz S et al reported mean scores of 1.76 and 1.30 following orthopaedic procedures, which was statistically significant in his study[8]. Among the complications, there was statistically significant difference in the incidence of postoperative shivering in Fentanyl group (16.7%) than Nalbuphine (3.3%) and p=0.04.

CONCLUSION

We conclude that intrathecal Fentanyl as an adjuvant to 0.5% Hyperbaric Bupivacaine was superior to Nalbuphine in the onset of both sensory and motor blockade. Nalbuphine is superior to Fentanyl for increasing the duration of postoperative analgesia and reduced requirement of rescue analgesia and reduced incidence of postoperative shivering.

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