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FENTANYL VERSUS NALBUPHINE AS ADJUVANT TO SPINAL BUPIVACAINE FOR CAESAREAN DELIVERY – A COMPARATIVE STUDY

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ABSTRACT

BACKGROUND: Local anaesthetics, commonly bupivacaine has been utilized for providing anaesthesia but alone are usually insufficient to provide uniform block despite the high level of anaesthesia. Several adjuvants have been added to local anaesthetics for prolongation of the duration of single shot spinal anaesthesia e.g. fentanyl, morphine, nalbuphine, etc.
AIM: This study was carried out to see the relative effectiveness of intrathecal fentanyl and intrathecal nalbuphine added to low dose intrathecal bupivacaine given for caesarean delivery.
MATERIALS AND METHODS: A total of 80 patients were randomly allocated to two groups of 40 each. Group A received 1.5 ml of 0.5% hyperbaric bupivacaine + 0.4ml fentanyl(20μg) + 0.1 ml distilled water. Group B received 1.5ml of 0.5 % bupivacaine + 0.4ml nalbuphine(0.8mg) + 0.1 ml distilled water. The groups were studied for assessing the quality of anesthesia and incidence of undesirable complications.
RESULTS: Sensory block characteristics like onset of sensory block is quite fast i.e. 1.85 min for fentanyl group and 1.50 min for nalbuphine group which is comparable, in 22(55%) patients in fentanyl group and 28(70%) patients in nalbuphine group the sensory block height reached T4 level. The fentanyl group has longer duration of analgesia/anaesthesia and motor blockade too is longer with the fentanyl group in comparison to the nalbuphine group. The occurrence of complications was comparable between the two groups.
CONCLUSION: Both drugs are effective as adjuvant to hyperbaric bupivacaine for spinal anaesthesia for caesarean section providing good quality surgical anaesthesia with practical absence of side effects but fentanyl scores over nalbuphine as far as prolongation of post-operative analgesia is concerned.

INTRODUCTION:

Regional anaesthesia is the anaesthesia of choice which is being administered for caesarean section deliveries. Local anaesthetics have been utilized for providing anaesthesia but alone are usually insufficient to provide uniform block despite the high sensory level of anaesthesia. Several adjuvants have been utilized to prolong the duration of single shot spinal anaesthesia which includes fentanyl, morphine, dexmedetomidine etc.[1]

Spinal anaesthesia with local anaesthetic agents, especially bupivacaine, has side effects such as hypotension, respiratory depression, vomiting and shivering in a dose dependent fashion. Hypotension is one of the commonest side effects and can affect both the mother and the neonate.[2] It is the local anaesthetic dose that is responsible for this complication. Adjuvants are drugs which increase the efficacy or potency of other drugs when given concurrently.[3] Intrathecal adjuvants are used to augment regional anaesthesia and also produce relatively fewer side effects which are manageable, example of intrathecal adjuvants include opioids and non-opioids.

Fentanyl is a lipophilic opioid with a rapid onset following intrathecal injection. When added to intrathecal bupivacaine in caesarean delivery, it improves quality of anaesthesia without producing significant side effects and improves post-operative analgesia and provides hemodynamic stability.[6]

Nalbuphine is a mixed agonist – antagonist opioid and has a potential to attenuate the mu-opioid effects and to enhance the kappa-opioid effects.[5] Nalbuphine when used as adjuvant to hyperbaric bupivacaine, has improved the quality of perioperative analgesia with fewer side effects It has potential to provide good intraoperative and post-operative analgesia with decreased incidence of mu receptor side effects.[6,7]

This study compares two opioids –one pure agonist and another agonist - antagonist when used as adjuvants to intrathecal bupivacaine given for caesarean delivery to see their relative effectiveness with regards to quality of anaesthesia, duration of sensory and motor blockade and any untoward complications.

MATERIALS AND METHODS:

After obtaining approval from the institutional ethical committee and informed consent from participating patients, this prospective, randomized and double blinded study was conducted in the Department of Anaesthesiology, Jawaharlal Nehru Institute of Medical Sciences, Manipur for a period of two years in 80 patients with American Society of Anaesthesiologists (ASA) physical status I and II patients, aged 20-45 years scheduled for caesarean section under spinal anaesthesia. Patients fulfilling the inclusion criteria were enrolled.

Inclusion criteria:

- Patient aged 20-45 years of age.

- American Society of Anaesthesiologists (ASA) physical status I and II.
- Normal coagulation profile.
- Scheduled for caesarean section under spinal anaesthesia.
- who had signed a written informed consent form.

Exclusion criteria:
- Patient refusal.
- Contraindication to spinal anaesthesia.
- History of allergy to study drugs.
- Systemic disease complicating pregnancy.
- Pregnancy-induced hypertension or eclampsia.

The patients were allocated to two groups: A and B following a restricted block randomization using a block size of 4. Group A received 1.5 ml of 0.5% hyperbaric bupivacaine + 0.4ml fentanyl(20µg) +0.1ml distilled water. Group B received 1.5ml of 0.5 % bupivacaine + 0.4ml nalbuphine (i.e. 0.8mg where 10mg/ml amp. diluted to 5 ml with distilled water; taking 0.4ml from the diluted solution which contained nalbuphine 2mg/ml) + 0.1 ml distilled water.

Pre anaesthetic check-up, detailed history, physical examination and basic investigations were performed. Injection ranitidine 50mg was given intravenously 45 minutes before spinal block, inj. ondansetron 4mg was given intravenously before spinal block. Baseline parameters such as pulse rate, non-invasive blood pressure (NIBP), RR and SPO2 were noted.

An 18G cannula was secured in the non-dominant hand and IV Ringer solution 10ml/kg/15min (preload) was given to all the patients before the spinal block. Spinal injection was performed in the left lateral position under strict aseptic conditions with 25G Quincke Babcock needle at L2/L3 or L3/L4 interspace. The patient was made to lie down in supine position with a block underneath the right flank; the table was tilted 15 degrees head down till the sensory block level reached subcostal margin in the epigastric region; then it was kept at level.

On completion of giving spinal injection, all patients were monitored for the following:
1. Heart rate, saturation and NIBP were recorded every 3 minutes for the first 15 minutes and every 15 mins until completion of surgery. Bradycardia was treated with 0.6mg atropine IV. Respiratory depression was defined as respiratory rate <8 breaths /min or SpO2< 94% on room air and treated with oxygen supplementation. IV mephentermine was given if the systolic pressure falls by 20% of the baseline or falls below absolute 100mm Hg.
2. A continuous ECG monitoring done till the end of surgery
3. The level of sensory block assessed by pin prick and motor assessed by Modified Bromage scale.
4. Urinary output was measured by keeping a urinary catheter in situ which was removed after 24 hrs.
5. Complications related to spinal block or drug allergy like hypotension, bradycardia, pruritus, nausea, vomiting, shivering, rash and bronchospasm were recorded and managed.

Post operatively patients were monitored for degree of sedation, level of block, respiratory rate, NIBP, PR, oxygen saturation, regression of sensory block and motor block were assessed every 15 min till complete recovery.

The duration of analgesia noted. Any complications were recorded and managed accordingly. The patients were shifted to the post-operative ward after complete recovery from sensory and motor blocks.

Study tools:
- Modified Bromage scale:

0- No motor block with full flexion of knees and feet
1- Just able to flex knees, full flexion of feet
2- Unable to flex knees, but some flexion of feet possible.
3- Unable to move legs/feet

RESULTS:

In the present study, the groups were studied for assessing the quality of anesthesia and incidence of undesirable complications. The results of our study are as follows:

1. Cardiovascular parameters:

(a) Heart rate:

It was observed that the heart rate remained almost unchanged at different time intervals throughout the study period for both the groups. There was no statistically significant difference in heart rate seen between the two groups.

(b)Systolic blood pressure (SBP):

There was slight decreased in systolic blood pressure at different intervals of time after spinal injection for both the groups. There was no statistically significant difference in the parameter.

(c) Diastolic blood pressure (DBP):

There was slight fall in diastolic blood pressure from baseline at different intervals of time after spinal injection. There was no statistically significant fall in DBP in both the groups.

2. Sensory Block:

(a) Onset time:

The onset time of sensory block of the fentanyl and the nalbuphine groups showed mean value of 1.08 minutes and 1 minute respectively. There was no statistically significant difference in the parameter.

(b) Sensory onset to T10:

Table 1 shows the sensory onset to T10 of the fentanyl and the nalbuphine groups giving mean values of 1.85 and 1.50 minutes respectively and there is statistically significant difference with a p value of 0.004. Nalbuphine (Group B) demonstrating faster sensory onset to T10.

Table 1: Table showing the comparison of sensory onset to T10 between the two groups

	GROUP				p Value	Significance
	GROUP A		GROUP B			
	Mean	Std. Deviation	Mean	Std. Deviation		
Sensory onset to T10(min)	1.85	0.53	1.50	0.51	0.004	Significant

© Height of block:

Table 2 shows the comparison of maximum height of block between the two groups with maximum number of patients reached level of T_4 i.e. 22(55%) patients in group A and 28(70%) patients in group B. There is no statistically significant difference.

Table 2: Table showing the comparison of maximum height of block between the two groups

		GROUP		Total	p Value	Significance
		GROUP A	GROUP B			
Maximum height of block	T2	1(2.5%)	1(2.5%)	2(2.5%)	0.319	Not Significant
	T3	2(5%)	3(7.5%)	5(6.25%)		
	T4	22(55%)	28(70%)	50(62.5%)		
	T5	12(30%)	8(20%)	20(25%)		
	T6	3(7.5%)	0(0%)	3(3.75%)		
Total	40(100%)	40(100%)	80(100%)			

(d) 2 segment sensory regression time:
The mean 2 segment sensory regression time of Group A and Group B were 49.35 and 48.90 minutes respectively. There was no statistically significant difference.

(e) Mean duration of analgesia:
Table 3 shows the comparison of mean duration of analgesia between the two groups were group A and group B had 125.80 and 103.90 minutes respectively. Fentanyl group has longer mean duration of analgesia and there is statistically significant difference with p value of <0.001.

Table 3: Table showing comparison of mean duration of analgesia between the two groups

(minutes)	GROUP				p Value	Significance
	GROUP A		GROUP B			
	Mean	Std. Deviation	Mean	Std. Deviation		
Mean duration of analgesia	125.80	18.71	103.90	14.81	<0.001	Significant

(f) Duration of anaesthesia:
Table 4 shows the duration of anesthesia produced by fentanyl and nalbuphine groups of 125.80 and 103.90 minutes respectively. Fentanyl group demonstrated greater duration of anaesthesia and there is statistically significant difference with p value <0.001

Table 4: Table showing the comparison of duration of anesthesia between the two groups

(minutes)	GROUP				p Value	Significance
	GROUP A		GROUP B			
	Mean	Std. Deviation	Mean	Std. Deviation		
Duration of anaesthesia	125.80	18.71	103.90	14.81	<0.001	Significant

4. Motor block:
(a) Motor block onset:
The mean motor block onset of Group A and Group B were 1.28 and 1.15 minutes respectively. There is no statistically significant difference.

(b) Duration of motor blockade:
Table 5 demonstrates the mean duration of motor blockade in fentanyl group and nalbuphine group of 99.10 and 83.65 respectively with fentanyl group having longer duration of motor blockade and there is a statistically significant difference with p value <0.001.

Table 5: Table showing the comparison of duration of motor blockade between the two groups

(minutes)	GROUP				p Value	Significance
	GROUP A		GROUP B			
	Mean	Std. Deviation	Mean	Std. Deviation		
Duration of motor blockade	99.10	14.47	83.65	15.57	<0.001	Significant

5. Complications:
Hypotension: the incidence of hypotension in the study groups with maximum incidence found in Group B i.e. 26(65%) with incidence of 21(52.5%) in Group A.

Nausea: Two patients developed nausea in Group B compared to none in Group A which is statistically not significant.

Vomiting: the incidence of vomiting in the two groups- nil in Group A and 1 in Group B. This is insignificant statistically.

Shivering: 1 patient in Group A and 2 in Group B had shivering which is statistically insignificant.

Respiratory depression: No patient in either group had respiratory depression.

Bradycardia: Only 1 patient in Group B had bradycardia as against none in Group A which is insignificant statistically.
Sedation: Incidence of sedation was nil in both groups

Statistical Methods :
- Categorical variables are expressed as number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test as appropriate.
- Continuous variables are expressed as Mean and Standard Deviation and compared across the groups using unpaired t test.
- The statistical software SPSS version 20 has been used for the analysis.
- An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant.

DISCUSSION:
Regional anaesthesia is the anaesthesia of choice which is being administered for caesarean section deliveries. Local anaesthetics have been utilized for providing anaesthesia but even with the standard dose of hyperbaric bupivacaine alone it is usually found insufficient to provide uniform block despite the high sensory level of anaesthesia. Several adjuvants have been utilized to prolong the duration of single shot spinal anaesthesia which includes fentanyl, morphine, etc.

Intrathecal adjuvants are used to augment regional anaesthesia and also produce relatively fewer side effects which are manageable. Intrathecal opioids bind to a family of G-protein-linked pre- and postsynaptic opioid receptors in Laminae I and II of the dorsal horn. Receptor activation leads to G-protein mediated potassium channel opening (mu and delta) and calcium channel closure (kappa), with an overall reduction in intracellular calcium decreasing the release of excitatory neurotransmitters decreasing C fibre nociception. Coadministration of opioids with central neuraxial local anaesthetics results in synergistic analgesia.

Fentanyl is a lipophilic opioid with a rapid onset following intrathecal injection. When added to intrathecal bupivacaine in caesarean delivery, it improves quality of anaesthesia without producing significant side effects and improves post-operative analgesia and provides hemodynamic stability.

Nalbuphine is a mixed agonist – antagonist opioid. Nalbuphine when used as adjuvant to hyperbaric bupivacaine, has improved the quality of perioperative analgesia with fewer side effects.

In our study, a total of 80 parturients were selected, 40 in each group randomly assigned in one of two groups:

Group A received 1.5ml of 0.5% hyperbaric bupivacaine + 0.4ml fentanyl(20μg) + 0.1ml distilled water.

GROUP B received 1.5ml of 0.5 % bupivacaine + 0.4ml nalbuphine(0.8mg) + 0.1 ml distilled water.

The rationale behind choosing fentanyl dose of 20mcg and nalbuphine dose of 0.8mg was ease of their preparation as both can be achieved as the content in 0.4 ml as such or after reconstitution. Intrathecal dose of fentanyl ranges from 10 mcg to 25 mcg in many previous studies while it ranges from 0.2mg to 1.2mg for nalbuphine. In terms of potency fentanyl is about 100 times as potent as morphine while nalbuphine is almost equipotent as morphine milligram for milligram. Equipotent dose of buprenorphine matching 20mcg of

fentanyl will be 2mg. But buprenorphine dose higher than 0.8mg offers no advantage when used as an adjuvant to hyperbaric bupivacaine for spinal anaesthesia for caesarean section. Adjuvant dose of 0.8mg for nalbuphine and 20mcg for fentanyl to 7.5mg hyperbaric 0.5% bupivacaine is a time-tested combination.

In our comparative study, the quality of anaesthesia and incidence of undesirable complications of hyperbaric bupivacaine in combination with fentanyl (20mcg) or nalbuphine (0.8mg) in patients undergoing caesarean section were observed and recorded. To be labelled as a good quality surgical anaesthesia produced by spinal block the resultant block should be intense with early onset of sensory block and the level reaching T_4 dermatome when we talk about spinal anaesthesia for caesarean section. Mother's satisfaction is to the maximum when she feels no discomfort during surgery and has a long pain free period post operatively.

In our study both fentanyl and nalbuphine adjuvants added to hyperbaric bupivacaine are effective to produce quality surgical anaesthesia for caesarean section. Sensory block characteristics like onset of sensory block is quite fast i.e. 1.85 min for fentanyl group and 1.50 min for nalbuphine group which is comparable, in 22(55%) patients in fentanyl group and 28(70%) patients in nalbuphine group the sensory block height reached T_4 level. The fentanyl group has longer duration of analgesia/anaesthesia (125.80min ± 18.71) and motor blockade too is longer in comparison to the nalbuphine group (103.90min ±14.81). However, contrary to our finding, Bindra TK et al[8] and Singh N et al[21] found a more prolonged analgesia in nalbuphine group than fentanyl group though the intrathecal dose of hyperbaric bupivacaine in their study was 10mg as against 7.5 mg of ours.

Our finding of prolongation of post-operative analgesia in both groups is in agreement with those of Singh N et al[21] and Bindra TK et al[8].There is prolongation of analgesia in the post-operative period delaying requirement of analgesia in the fentanyl group which is consistent with those of Gopichand K et al[17] and Gauchan S et al[18].

The longer duration of post-operative analgesia in the fentanyl group in our study correlates with that of Prabhakariah UN et al.[13]

As for complications associated with the spinal block all cardiovascular and respiratory parameters remained intact throughout the study period apart from slight fall of blood pressure at certain time interval. We can claim that there is haemodynamic stability. And as for undesirable effects associated with opioid therapy only occasional incidence of nausea or vomiting was observed but it was conspicuous by the absence of sedation, respiratory depression, itching. Incidence of urinary retention and constipation could not be ascertained.

Finally, our aim of establishing the effectiveness of adjuvant doses of both fentanyl and nalbuphine is achieved without subjecting the mother to undue risk.

The limitations of our study were we did not have control group but we did have a better surgical anaesthesia using low dose bupivacaine with minimal side effects.

CONCLUSION:

From the results of the study, it can be concluded that:

1. Both fentanyl and nalbuphine are effective as adjuvant to hyperbaric bupivacaine for spinal anaesthesia for caesarean section providing good quality surgical anaesthesia.
2. Fentanyl scores over nalbuphine as far as prolongation of post-operative analgesia is concerned.
3. With practical absence of complications/side effects it can be stated to be safe for both the mother and the new-born.

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