COMPARISON OF INTRATHECAL NALBUPHINE VS FENTANYL ADDED TO 0.5% HYPERBARIC BUPIVACAINE FOR PERIOPERATIVE ANAESTHESIA AND PERIOPERATIVE / POST OPERATIVE ANALGESIA IN HERNIOPLASTY- PROSPECTIVE STUDY

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ABSTRACT :

Background Nalbuphine is synthetically prepared opioid. It has both κ agonist and μ antagonist properties(13). When given intrathecally it binds to kappa receptors in the spinal cord and brain. It produces analgesia and sedation via kappa receptors and hence there is no adverse effects mediated by μ receptors. In this study we compared the effectiveness of the two adjuvants nalbuphine and fentanyl added to 0.5% hyperbaric bupivacaine in patients undergoing hernioplasty as Group A and Group B respectively, along with a control group C of intrathecal bupivacaine alone with normal saline.
Methods: This study was done in mookambikai medical college hospital,at Department of Anaesthesiology and critical care from December 2023 to September 2024.It was a Single centre, prospective, randomized double blinded, interventional controlled study**.** Inclusion criteria are ,20 - 60 years of age,ASA physical status I or II,Patients who gave valid informed written consent,Patients undergoing elective hernioplasty.Exclusion criteria is considered as Patients having any absolute contraindications for spinal anaesthesia,Infection at the subarachnoid block injection site,Patients with neurological and musculoskeletal disease,
Results: fentanyl significantly shortens the time of onset of sensory block when to compared to nalbuphine. The mean onset time of sensory block (T10) in the nalbuphine group was found to be 3.05±0.88 mins, in fentanyl group it is 2.25±0.63 mins ,whereas in the control group it was found to be 4.08±1.25 mins. In Fentanyl group the mean time of onset of sensory block was 0.80mins earlier than nalbuphine group. C.

Conclusion: Comparing between Intrathecal Nalbuphine and Fentanyl concludes that: Intrathecal Nalbuphine may be a good alternative to Fentanyl in surgeries like hernioplasty and in below umbilical surgeries which provides a prolonged sensory and motor blockade, and prolonged duration of analgesia without any adverse effects
Keywords: Hernioplasty, Hyperbaric Bupivacaine.

INTRODUCTION:

In 1898, August Bier first described "cocainisation of the spinal cord". The technique has been refined over the years and has evolved into the modern concept of intrathecal, spinal or subarachnoid block. One of the most commonly performed technique in modern anaesthesia is Central neuraxial blockade.

In surgeries like hernioplasty the most preferred regional anaesthesia is spinal anaesthesia. Spinal anaesthesia produces dense motor, sensory and sympathetic blockade. Subarachnoid block is a preferred technique in patients who are prone to aspiration like obesity, full stomach, GERD and in patients with reduced respiratory drive. Spinal anaesthesia reduces mortality and morbidity in high risk surgical patients.

Simplicity to perform and more rapid onset with good sensory as well motor block(1), excellent analgesia and decreased stress response to surgery and intra operative blood loss have made spinal anaesthesia preferable in infraumbilical surgeries like hernioplasty. Most commonly used amide local anaesthetic bupivacaine produces prolonged intense sensory and motor block with significant sympathetic blockade and excellent surgical relaxation(2, 3). Normally, spinal anaesthesia with hyperbaric bupivacaine lasts for 2 to 2.5 hours(4). Commonly used dosage, it produce more undesirable side effects(5): By reducing the dosage of bupivacaine, limits its distribution of spinal block, and it causes comparably rapid recovery(6).
Various adjuvants are added to the local anaesthetics intrathecally, to prolongate the duration of anaesthesia. Adjuvants not only reduce the undesirable hemodynamic effects of spinal anaesthesia, by lowering the requirement of local anaesthetic dose, but also provide satisfactory block(7,8).

Among the adjuvants the most commonly preferred are the opioids. These adjuvants have “synergistic anti-nocioceptive effect” along with intrathecal local anaesthetic both during intra operative and post operative periods by extending analgesia duration(9). Opioids act at the receptor site in the spinal cord(10) and the local anaesthetics have their action at the spinal nerve axon. In 1979, Wang and his colleagues(11) first used intrathecal opioids for acute pain treatment. Since then, intrathecal opioid is widely used to increasethequality of Intraoperative anaesthesia, prolongthe postoperative analgesia, traumatic and chronic cancer pain.
Administration of intrathecal opioid along with local anaesthetics is to improve the quality of analgesia and to decrease the requirement of postoperative analgesics(12). Various opioidshave been used intrathecally like morphine, fentanyl, buprenorphine and nalbuphine to fasten the onset and prolong the duration of sensory and motor blockade.

Nalbuphine is synthetically prepared opioid. It has both κ agonist and μ antagonist properties(13). When given intrathecally it binds to kappa receptors in the spinal cord and brain. It produces analgesia and sedation via kappa receptors and hence there is no adverse effects mediated by μ receptors. Side effects like shivering, nausea, vomiting and urinary retention are infrequent with nalbuphine hydrochloride. Nalbuphine reaches ceiling effect at lower intrathecal dosage and so no need to increase the dosage.
Fentanyl is a lipophilic μ receptor opioid agonist. Intrathecal fentanyl as adjuvant to local anaesthetic has a rapid onset of action and significantly reduces visceral and somatic pain which have been proved in various studies(14, 15).

Although there are several studies that includes comparison of Nalbuphine and fentanyl as adjuvant, there is no particular study in patients undergoing hernioplasty.
In this study we compared the effectiveness of the two adjuvants nalbuphine and fentanyl added to 0.5% hyperbaric bupivacaine in patients undergoing hernioplasty as Group A and Group B respectively, along with a control group C of intrathecal bupivacaine alone with normal saline.

AIM AND OBJECTIVES OF THE STUDY:

The aim of the study was to Compare intrathecal nalbuphine vs fentanyl added to 0.5% hyperbaric bupivacaine for perioperative anaesthesia and postoperative analgesia in patients undergoing hernioplasty.

Sensory block onset time (sensory level T10) , Motor block onset time(Bromage 3)
Highest level of sensory block reached and time taken to reach it.Time taken for two segment regression of

sensory level Duration of motor block Duration of analgesia.

MATERIALS AND METHODS:

This study was done in mookambikai medical college hospital,at Department of Anaesthesiology and critical care from December 2023 to September 2024.
It was a Single centre, prospective, randomized double blinded, interventional controlled study.After obtaining institutional ethical committee approval, 120 patients posted for elective hernioplasty surgery under spinal anaesthesia with satisfying inclusion criteria were enrolled in the study after obtaining informed consent from the patients and relatives.

Inclusion criteria are ,20 - 60 years of age,ASA physical status I or II,Patients who gave valid informed written consent,Patients undergoing elective hernioplasty.
Exclusion criteria is considered as Patients having any absolute contraindications for spinal anaesthesia,Infection at the subarachnoid block injection site,Patients with neurological and musculoskeletal disease,Patients with bleeding disorders,Patients on anticoagulants,History of allergy to local anaesthetics and Obese patients (obesity BMI > 30kg/m2).
All the patients were duly examined on the day prior to surgery and pre-operative assessment sheet was checked. The height (cms), weight(kg), body mass index(BMI), of the patient were measured. The airway assessment, spine examination and the nutritional status of the patient were evaluated. A detailed general and systemic examination was done. Preoperative investigations like complete haemogram (CBC), renal function tests(RFT), random blood sugar, blood grouping and typing,
coagulation profile, electrocardiography and chest X ray were evaluated properly.

Statistical analysis was done using the statistical package for social sciences (SPSS).Different statistical methods were used as appropriate. Mean ± SD was determined for quantitative data and frequency for categorical variables. The independent t- test was performed on all continuous variables. The normal distribution data was checked before any t-test. The Chi-Square test was used to analyze group difference for categorical variables. A p- value < 0.05 was considered significant.

RESULTS:

All 120 patients with ASA physical status I/II who satisfied all inclusion criteria were randomly divided into three groups and underwent Hernioplasty under subarachnoid block in all the patients completed the study without any exclusion.
The collected data were analyzed by one-way ANOVA and results obtained in form of mean and standard deviation. The probability value $p <$
0.05 is considered as statistically significant. comparison of the resuts :

Comparison of Time to reach highest level of sensory block:

THSL	N	Mean	Std. Deviation	P value
Group A	40	13.75	2.06	
Group B	40	11.68	2.44	
Group C	40	14.54	3.54	
Total	120	12.92	2.87	0.002

Comparison of mean time to reach highest sensory level among three Groups is statistically significant (P value0.002). Time to reach highest sensory level of Group B is much earlier than Group A and it is statistically significant (P value 0.003). Time to reach highest sensory level of Group A is earlier than Group C and it is not statistically significant.
Comparison of mean time for two segment regression of sensory level among three Groups:

		N	Mean	Std. Deviation	P value
TRSL	Group A	40	90.40	13.79	
	Group B	40	81.35	6.77	
	Group C	40	50.98	3.58	
	Total	120	74.24	19.19	<0.0001

Tab.9.TRSL comparison

Dependent Variable				Mean Difference (I-J)	P value
TRSL	Group A	Group B	9.05	0.000	
		Group C	39.43	0.000	
	Group B	Group A	-9.05	0.000	
		Group C	30.38	0.000	

	Group C	Group A	-39.43	0.000
		Group B	-30.38	0.000

Comparison of mean time for two segment regression of sensory level among three groups is statistically significant (P value <0.0001). Mean time for two segment regression of sensory level of Group A is much higher than Group B and it is statistically significant (P value 0.000). Mean time for two segment regression of sensory level of Group B is higher than Group C and it is statistically significant (P value 0.000).

Comparison of mean time of onset of motor block

		N	Mean	Std. Deviation	P value
MOT	Group A	40	2.33	0.69	
	Group B	40	1.48	0.51	
	Group C	40	3.43	0.93	
	Total	120	2.41	1.08	<0.0001

.MOT comparison

Dependent Variable			Mean Difference (I-J)	P value
MOT	Group A	Group B	0.85	0.000
		Group C	-1.10	0.000
	Group B	Group A	-0.85	0.000
		Group C	-1.95	0.000

	Group C	Group A	1.10	0.000
		Group B	1.95	0.000

Comparison of highest sensory level reached among three Groups:

		HSL					Total	P value
		T2	T3	T4	T5	T6		
group	Group A	14	0	22	4	0	40	<0.0001
	Group B	2	2	20	16	0	40	
	Group C	0	0	1	8	31	40	
Total		16	2	43	28	31	120	

Comparison of duration of analgesia:

		N	Mean	Std. Deviation	P value
DOA	Group A	40	5.15	.350	<0.0001
	Group B	40	4.05	.539	
	Group C	40	2.64	.349	
	Total	120	4.36	4.702	

Comparison of side effects observed during study :

		Complication				Total	P value
		Nil	Bradycardia	Hypotension	Shivering		
group	Group A	34	3	2	1	40	0.573
	Group B	34	4	2	0	40	
	Group C	34	2	1	3	40	
Total		102	9	4	4	120	

.MOT multiple comparison

Dependent Variable			Mean Difference (I-J)	P value
postop_sbp	Group A	Group B	-0.27	1.000
		Group C	-4.55	0.024
	Group B	Group A	0.27	1.000
		Group C	-4.28	0.038
	Group C	Group A	4.55	0.024
		Group B	4.28	0.038
postop_dbp	Group A	Group B	-0.05	1.000
		Group C	-1.70	0.089
	Group B	Group A	0.05	1.000
		Group C	-1.65	0.104
	Group C	Group A	1.70	0.089
		Group B	1.65	0.104
postop_hr	Group A	Group B	-0.55	1.000
		Group C	-2.10	0.079
	Group B	Group A	0.55	1.000
		Group C	-1.55	0.299
	Group C	Group A	2.10	0.079
		Group B	1.55	0.299

Postop vitals multiple comparison

Comparing the postoperative vitals among the three groups, the systolic and diastolic Bp are statistically significant with p value 0.012 & 0.047 respectively. PR, spo2 are not statistically significant.

DISCUSSION:

Extensive research have been done over the years mainly to improve the quality of spinal anaesthesia simply by varying drug regimens and technical methods. Normally to prolong the anaesthetic effects adjuvants are added to hyperbaric bupivacaine 0.5% and given intrathecally. Adjuvants produce antinociceptive effect by acting perineurally or by acting at different receptor sites in the spinal cord.
Adjuvants mainly opioids are capable of producing early onset of sensory and motor blockade and also prolongs the postoperative analgesia. They also have sympathetic and motor sparing activities which allows early ambulation of patients postoperatively.

Nalbuphine hydrochloride is a mixed μ antagonist and κ agonist opioid. Nalbuphine has been found

to cause prolongation of the effects of local anaesthetics in intrathecal, epidural and also in peripheral nerve blocks and it has the advantages of minimal respiratory depression and better hemodynamic stability.
Various studies had been done using 25mcg of fentanyl added to 0.5% hyperbaric bupivacaine which administered intraathecally for various surgeries, including gynaecological surgeries/lower limb surgeries/lower abdominal surgeries/caesarean section and revealed the efficacy and safety of intrathecal fentanyl.

Intrathecal fentanyl and nalbuphine hydrochloride was in practice over many years and found to be safe and effective and has no neurotoxic side effects when used intrathecally.
Mukherjee et al performed a study to determine whether Nalbuphine hydrochloride is safe and whether it helps to prolongs analgesia by comparing it with control group and also to determine the optimum dose of intrathecal nalbuphine'. They observed that 0.4mg of nalbuphine + 0.5% hyperbaric bupivacaine prolongs the duration of postoperative analgesia without any side effects. Hence we used 0.5mg of nalbuphine intrathecally.

In my study, fentanyl significantly shortens the time of onset of sensory block when to compared to nalbuphine. The mean onset time of sensory block (T10) in the nalbuphine group was found to be 3.05±0.88 mins, in fentanyl group it is 2.25±0.63 mins ,whereas in the control group it was found to be 4.08±1.25 mins. In Fentanyl group the mean time of onset of sensory block was 0.80mins earlier than nalbuphine group. Comparison of mean time to reach highest sensory level among three Groups is statistically significant (P value0.002). Time to reach highest sensory level of Fentanyl group was (11.68±2.44 mins) much earlier than nalbuphine Group (13.75±2.06 mins) and it is statistically significant (P
value 0.003).Early onset and earlier to reach highest sensory level of
just because of highly liphophillic nature of fentanyl. Mean duration of motor blockade in the nalbuphine group was 3.41±0.322 hrs, in the fentanyl group it is3.19±0.747hrs and in the control group was 1.97±0.358 hrs which was statistically significant(p value <0.0001). Mean duration of motor blockade in nalbuphine group is higher than fentanyl group.

Study conducted by Ravikiran J Thote et al., (33) , and the study conducted by Pallavi Ahluwalia et al., (37) concludes similar results. However Hala Mostafa Gomaa et al., (36) concludes that there is no statistically significant difference in the duration of motor blockade between intrathecal nalbuphine and fentanyl.
The mean duration of analgesia in the nalbuphine group was found to be 5.15±.350 hrs , in fentanyl group was 4.05±.539hrs and in the control group it was found to be 2.64±0.349hrs which was statistically significant (p value <0.0001) between the three groups.

The results that obtained in our study reveals that duration of analgesia is much prolonged by intrathecal nalbuphine than fentanyl.Study conducted by Ravikiran J Thote et al., (33) also concludes that intrathecal nalbuphine prolongs the duration of analgesia than intrathecal fentanyl. Shehla shakooh,et al., (33) study also concludes that sensory blockade ,motor blockade and post operative analgesia was
much prolonged with intrathecal nalbuphine group than plain bupivacaine group. Mukherjee et al., (33)2011 study concluded that 0.4mg nalbuphine is the most effective intrathecal dose that increases postopertative analgesia with no side sffects. Gurunath BB et al., (39) Study also cocludes that the nalbuphine group had much prolonged duration of postoperative analgesia than fentanyl group.

Comparison of mean systolic blood pressure among Group A, Group B, Group C is statistically significant at 0min($p<0.026$),3min($p<0.002$), 6min($P<0.012$), 9min ($p<0.018$) and 45min($p<0.0001$). In multiple comparison the mean SBP of nalbuphine Group A is higher than fentanyl Group B & control group C at 0,3,6,45 min. SBP of Group A is lower than Group B & C at 9min and it is statistically significant($p<0.018$). Comparing the mean diastolic BP of three groups is statistically significant at 6min ($p<0.003$) and 30min ($p<0.004$). In multiple comparison, Mean Diastolic Bp at 6min of Group A is higher than Group B which is statistically significant($p <0.004$) and also Group C is higher than Group B which is statistically significant($p <0.022$). Mean Diastolic Bp at 30min of Group A is higher than Group C (not statistically significant) & also Group C is higher than Group B (statistically significant $p<0.004$). Comparison of pulse rate between three groups at 6min ($p<0.016$) and 12min ($p<0.002$) are statistically significant.

Mean pulse rate of Group A at 6min 73/min, at 12min 72/min ,Group B at6min 69/min,at12min 67/min, andGroup C at 6min 68/min, at 12min 69/min.Comparing the postoperative vitals among the three groups, the systolic and diastolic Bp are statistically significant with p value< 0.012 &< 0.047 respectively. PR, spo2 are not statistically significant. Though statistically significant variation was noted in haemodynamic parameters like non invasive blood pressure(NIBP)/HR/spo2periodically both intraoperative and postoperative period among the three groups, all patients were haemodynamically stable in all three groups. Intrathecal opioids intensifies the sensory block without increasing sympathetic block just because they are synergistic with local anaesthetics. Our results are similar to the results concluded by Hala Mostafa Gomaa et al study., (36):

Bradycardia and hypotension observed was treatable and it was mainly due to the sympathetic blockade of the local anaesthestics itself and not by the adjuvants added. Shivering was observed more in control group than the nalbuphine group. Side effects observed during our study was very minimal and most of the cases were stable and it is not statistically significant. Various studies conducted concludes the safety and effectiveness of nalbuphine and fentanyl when added intrathecaliy.blockade by fentanyl group may be explained due to high lipid solubility of fentanyl which makes it to cross blood brain barrier easily and also rapid tissue uptake. Similar result was obtained by the study conducted by Gurunath BB et al., (39) in 2018 and study conducted by Ravikiran J Thote et al., (33) However the study conducted by Hala Mostafa Gomaa et al., (36) concluded that there is no significant difference between intrathecal nalbuphine and fentanyl regarding to the sensory blockade.

More number of patients in the nalbuphine group (A) achieved higher sensory level (T2 toT4) than the patients in the fentanyl Group(B) (T2 to T5). The mean time for two sement regression of sensory block in the nalbuphine group was found to be 90.40±13.79 mins and in fentanyl group B was 81.35±6.77 mins whereas in the control group it was found to be 50.98±3.58 mins. Higher sensory level and more prolongation of two segment regression of sensory blockade by intrathecal nalbuphine than intrathecal fentanyl was concluded by the studies conducted by Ravikiran J Thote et al., (33) Gurunath BB et al., (39) , Shehla Shakooh et al (30), and by Jyothi B et al., (30).

The mean onset time of motor block was found to be 2.33±0.69 mins in the nalbuphine group, 1.48±0.51 mins whereas in the control group it was found to be 3.43±0.93 mins. Similar to sensory blockade the onsetof motor blockade is much earlier in fentanyl group than nalbuphine group.

CONCLUSION:

Comparing between Intrathecal Nalbuphine and Fentanyl concludes that: Intrathecal Nalbuphine may be a good alternative to Fentanyl in surgeries like hernioplasty and in below umbilical surgeries which provides a prolonged sensory and motor blockade, and prolonged duration of analgesia without any adverse effects.

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