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COMPARISON OF INTRATHECAL NALBUPHINE VERSUS KETAMINE AS AN ADJUVANT TO HYPERBARIC BUPIVACAINE IN INFRAUMBILICAL SURGERIES

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ABSTRACT **Background and aim:** Hyperbaric bupivacaine is the most common drug used in spinal anaesthesia but the drawback is limited duration of analgesia when performed with local anaesthetics alone.Nalbuphine and Ketamine added to hyperbaric bupivacaine as adjuvants tend to prolong the duration of postoperative analgesia.In this study, comparison of Nalbuphine versus Ketamine as an adjuvant to hyperbaric Bupivacaine for duration of postoperative analgesia, onset of sensory and motor block, haemodynamic stability, side effects and VAS score was done.**Materials and methods:** Fifty four patients of ASA grade I and II undergoing elective infraumbilical surgeries were studied prospectively and were randomly divided in two groups N and K who received 3ml hyperbaric bupivacaine with 0.8 mg nalbuphine in 0.5ml saline and 3ml hyperbaric bupivacaine with 25mg ketamine in 0.5ml respectively.Results: There was a significant difference in onset of sensory block between groups N and K with earlier onset in group N.Mean duration duration of analgesia in group N was prolonged in comparison to group K.There was statistically insignificant difference between onset of motor block and total duration of motor blockade.**Conclusion:** Nalbuphine proves to be a better adjuvant than Ketamine with respect to onset of sensory block, duration of analgesia and haemodynamic stablity with minimal side effects.

KEYWORDS : Ketamine, Nalbuphine, analgesia.

INTRODUCTION:

Spinal anaesthesia with hyperbaric Bupivacaine is the most common and widely accepted technique for the patients undergoing lower limb, perineal and lower abdominal surgeries.Spinal anaesthesia is a simple technique that has benefits of sensory and motor blockade, good muscle relaxation and no loss of consciousness.[1]However, limited duration of analgesia, bradycardia, systemic hypotension, etc. are some undesirable side effects adding to its limitations.

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage.The surgical stress response is maximum in the immediate postoperative period and is associated with adverse outcomes like ventilatory depression, tachycardia, hypertension, endocrine disorders,etc.[1]The prevention and management of pain is an important aspect of patient management.Various adjuvants like Midazolam, opioids, α-2 adrenergic agonists, Ketamine, Neostigmine, etc. have been added to local anaesthetics administered intrathecally to increase the duration and quality of sensory blockade and prolongation of postoperative analgesia.[2]

Nalbuphine is a semi-synthetic opioid belonging to phenanthrene series with μ receptor antagonist and κ receptor agonist property, when administered intrathecally as an adjuvant provides prolongation of analgesia without prolongation of motor blockade with limited side effects such as nausea, vomiting, sedation, pruritus or respiratory depression.It acts by reducing the release of GABA and glycine from dorsal horn neurons.[1,2,3]It reduces intrathecal release of gamma amino butyric acid and glycine by a calcium-independent process from dorsal horn neurons.[2]

Ketamine, an analogue of phencyclidine acts by noncompetitive antagonism of NMDA receptor.The analgesic property is due to action on calcium and sodium channels, dopamine receptors, cholinergic trnasmission and noradrenergic and serotonergic reuptake with some anti-inflammatory effect.[1]Ketamine stimulates the cardiovascular system and does not alter respiratory response to carbon dioxide validating its beneficial effects on these systems with analgesic effect of spinal anaesthesia.[4]Ketamine provides better analgesia and cardiovascular stability when administered intrathecally.

This study was aimed to compare the effects of intrathecal adjuvants-Nalbuphine or Ketamine to hyperbaric Bupivacaine (0.5%) in infraumbilical surgeries in terms of onset of sensory and motor blockade, duration of analgesia and side effects.

MATERIALS AND METHODS:

After approval from institutional ethical committee, this study had been conducted over 54 patients belonging to 18 to 65 years of age, of either sex and of American Society of Anaesthesiologists grade I or II.The sample size was calculated by openepi software version 4 with the power of 80% and confidence interval of 95% from the mean number of rescue analgesia doses required as suggested by Amar Prakash Kataria et al.[1]The exclusion criteria for the study were as follows: Patient's refusal to participate in study, coagulation disorders, signs of neurological disease, signs of sepsis, spine deformity or history of spine surgery, morbid obesity, pregnancy and lactation, history of allergy to study drug and infection at local site of puncture.

All the patients enrolled in this study underwent thorough pre-anesthetic checkup before the surgery.The patients were kept fasting for 8 hours on the night prior to surgery.In the recovery room, baseline vitals like pulse, systolic and diastolic blood pressure, respiratory rate and SpO2 were recorded as well as written and informed consent was taken after explaining the patient about the procedure.

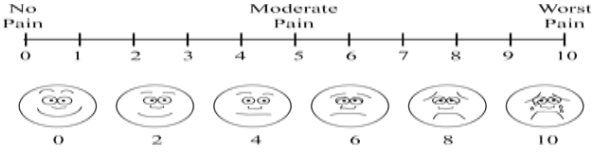
The patients were randomly divided into two groups viz patients of **Group N** were administered 3 ml (15 mg) of hyperbaric Bupivacaine (0.5%) with Nalbuphine 0.8 mg diluted in 0.5 ml normal saline whereas the patients of **Group K** were administered 3 ml (15 mg) of hyperbaric Bupivacaine (0.5%) with Ketamine 25 mg.This lead to total volume of 3.5 ml for each patient.

After securing intravenous access, injection Ringer's lactate solution was given at 10ml/kg body weight for preloading.In the operating room, multipara monitor was attached to the patient and heart rate, noninvasive blood pressure, SpO2, respiratory rate and electrocardiogram (ECG) were recorded.Premedication was given to all the patients with injection Glycopyrrolate 0.2 mg and injection Midazolam 0.04 mg/kg body weight intravenously.Spinal anaesthesia was given under all aseptic and antiseptic precautions in sitting position by midline approach at L2-L3 or L3-L4 intervertebral space by 25 G Quincke's needle.After verifying the free flow of CSF, the study drug was administered intrathecally and the patient was placed immediately in supine position.The anaesthesiologist who performed the technique recorded the intraoperative data and followed up in the postoperative period.

Heart rate, systolic blood pressure, diastolic blood pressure were recorded before lumbar puncture and then at every 2 minutes for 10 minutes, at every 5 minutes upto 30 minutes, at every 15 minutes upto

120 minutes and every 30 minutes upto 240 minutes after intrathecal injection of the study drug.Sensory block was assessed by pinprick method every 2 minute interval in midclavicular line on both sides until it gets stablised.Time to onset of sensory blockade was from the time of injection of study drug into intrathecal space to the time to loss of pinprick sensation at T10 level and the highest dermatome that achieved analgesia after subarachnoid block was the maximum level of sensory blockade.The sensory blockade was then assessed at every 30 minutes for two segment regression and regression to S1, postoperatively.Motor blockade was assessed by modified Bromage scale as follows-Grade 1: complete motor block, Grade 2: able to move feet only, Grade 3: able to move feet and knees, Grade 4: detectable weakness of hip flexion while supine, Grade 5: no detectable weakness of hip flexion while supine and Grade 6: able to perform partial knee bend; at similar time intervals as that of sensory blockade and regression of motor blockade to modified Bromage grade 6, postoperatively. Time to first rescue analgesia i.e. Injection Diclofenac sodium 75 mg intravenously in minutes when VAS>4 [FIGURE:1].Sedation was assessed by Ramsay sedation score-1: anxious or restless or both,2: Cooperative, oriented and tranquil,3: responding to commands only,4: brisk response to light glabellar tap or loud auditory stimulus,5: sluggish response to light glabellar tap or loud audutary stimulus,6: no response to stimulus.[1]Side effects like hypotension, nausea, vomiting, sedation, bradycardia, pruritus, etc were observed and recorded, if any.

FIGURE1:VISUALANALOG SCALE



STATISTIALANALYSIS:

All the data were analysed by using openepi software and all the quantitative data was analysed by paired student t-test and qualitative data by chi-square test. P<0.05 was considered to be significant and p<0.001 to be highly significant and p>0.05 was considered to be insignificant.

OBSERVATION AND RESULTS:

Patient demographic data were comparable in both the groups (p>0.05)[TABLE 1]. The heart rate, systolic blood pressure and diastolic blood pressure was stable intraoperatively and postoperatively were comparable in both the groups (p>0.05) [FIGURE 2][FIGURE 3][FIGURE 4].

TABLE 1:COMPARIS0N OF DEMOGRAPHIC DATA

DEMOGRAPHIC PROFILE			
PARAMETERS	MEAN±SD		P-VALUE
	GROUP N	GROUP K	
AGE (IN YEARS)	31.888±4.885	32.185±4.788	0.822
SEX (M/F)	15/12	13/14	
WEIGHT (IN KG)	66.555±4.870	65.037±5.382	0.280
DURATION OF SURGERY (IN MINS)	118.888±12.734	114.629±13.571	0.238

Data are presented as mean±SD or absolute numbers.SD-Standard deviation.

Time to onset of sensory blockade at T10 level was 2.19±0.20 minutes in Group N and 3.50±0.27 minutes in Group K (p<0.001) and the difference was statistically highly significant.Time to maximum sensory blockade level achieved was 6.05±0.31 minutes in Group N and 6.65±0.35 in Group K (p<0.001) and the difference was statistically highly significant.There was earlier onset of sensory blockade and time to achieve maximum level of sensory blockade in Group N as compared to Group K.The time to achieve maximum motor blockade was 7.09±0.33 minutes in Group N and 7.19±0.45 minutes in Group K that was not statistically significant (p>0.05)[TABLE 2].

Time to two segment regression in Group N was 76.33±4.4 minutes and 72.25±5.81 minutes in Group K that was statistically significant (p<0.05).Time to sensory regression to S1 in Group N was 184.22±6.09 minutes and 177.70±7.98 minutes in Group K that was statistically significant (p<0.05).The time to two segment regression and sensory regresssion to S1 level was prolonged in Group N as compared to Group K.There was no statistically significant difference in total duration of motor blockade between the two groups that was 205.18±6.71 minutes in Group N and 205.55±10.59 minutes in Group K (p>0.05).Time to first request to rescue analgesia was 297.4±8.10 minutes in Group N and 242.22±13.75 minutes in Group K and the difference between the two groups was highly significant (p<0.001) that was prolonged in Group N [TABLE 2].

Hypotension was observed in 1 (3.70%) patient in Group N and Group K each.Nausea was observed in 1 (3.70%) patient in Group N and 1 pateint (3.70%) in Group N had developed bradycardia.No sedation was observed in any of the patients.

TABLE 2: COMPARISON OF BLOCK CHARACTERISTICS

PARAMETERS	MEAN±SD		P-VALUE
	GROUP N	GROUP K	
TIME TO ONSET OF SENSORY BLOCK AT T10	2.19±0.20	3.50±0.27	<0.0000001
TIME TO MAXIMUM SENSORY BLOCKADE	6.05±0.31	6.65±0.35	<0.0000001
TIME TO MAXIMUM MOTOR BLOCKADE	7.09±0.33	7.19±0.45	0.35
TIME TO TWO SEGMENT REGRESSION	76.33±4.40	72.25±5.81	0.005
TIME TO SENSORY REGRESSION TO S1	184.22±6.09	177.70±7.98	0.001
TOTAL DURATION OF MOTOR BLOCKADE	205.18±6.71	205.55±10.59	0.8
TIME TO REQUEST FOR RESCUE ANALGESIA	297.4±18.10	242.22±13.75	<0.0000001

Data are presented as mean±SD, SD is standard deviation.

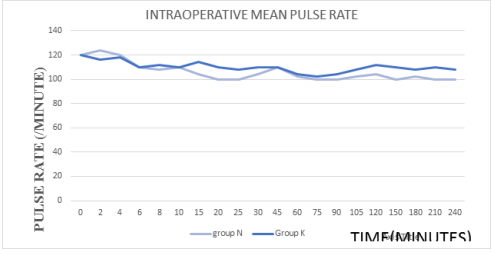


Figure 2: Comparison Of Intraoperative Pulse Rate

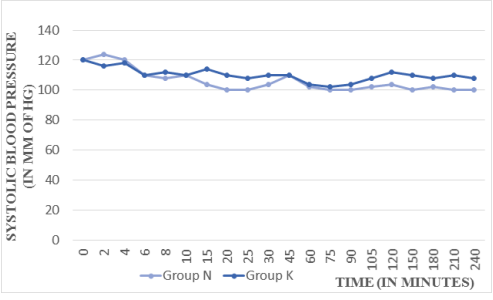


Figure 3: Intraoperative Mean Systolic Blood Pressure

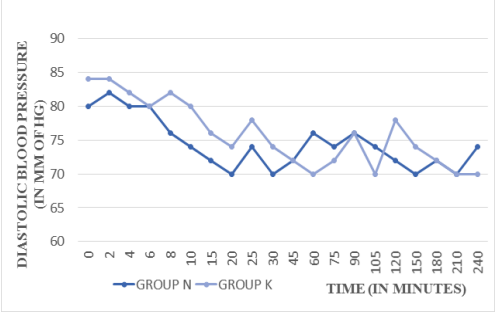


Figure 4: Intraoperative Mean Diastolic Blood Pressure

DISCUSSION:

Optimum care of the patient requires effective pain management in the postoperative period which helps alleviating pain and shortens the recovery time.Spinal anaesthesia with local anaesthetic agents being a simple, widely accepted and effective way for infraumbilical surgeries, addition of adjuvants like opioids, Ketamine, Midazolam, etc. enhances its block characteristics and duration of analgesia.[1]

In our study, Nalbuphine 0.8 mg or Ketamine 25 mg was added as an adjuvant to 3 ml of hyperbaric Bupivacaine 0.5% to evaluate sensory and motor block characteristics and duration of postoperative analgesia alongwith haemodynamic monitoring. Ketamine may diffuse into venous circulation of spinal cord and results in cardiovascular stimulation that anatagonises spinal anaesthesia induced vasodilatation.[5]

In our study, there was an faster onset of sensory blockade at T10 and early achievement of maximum sensory level in group N that was statistically highly significant.Amar Prakash Kataria et al[1] in 2018 had conducted similar study in lower abdominal surgeries under spinal anaesthesia and concluded that both ketamine and nalbuphine provided adequate analgesia and haemodynamic stability when added as an adjuvant, but Nalbuphine was better than Ketamine in earlier onset of sensory blockade and prolongation of analgesia and duration of sensory blockade with fewer side effects.The results of this study were in accordance to our study.In 2018, Aparna Jayara et al[3] had conducted a comparative study of analgesic effect of Nalbuphine and Tramadol in patients undergoing vaginal hysterectomy and concluded that time to reach T_{10} sensory level and peak sensory level was shorter in Nalbuphine group and their findings corroborated with our study.

The time for maximum motor blockade and total duration of motor blockade was comparable between both the groups and the difference was nonsignificant.The study conducted by Amar Prakash Kataria in 2018[1], it was observed that onset of motor blockade was early in Nalbuphine group as compared to Ketamine group but the difference was insignificant and the difference between the total duration of motor block was also insignificant as observed in our study.Similar time of onset of maximum motor blockade was observed in the study conducted by Aparna Jayara et al[3] in 2018.In 2018, Tridip Borah et al[2] had conducted study of effect of adding differennt dose of Nalbuphine 0.4 mg, 0.8 mg and 1.6 mg to 22.5 mg of isobaric ropivacaine intrathecally and found similar time to onset of motor blockade in Nalbuphine 0.8 mg group and also concluded 0.4 mg and 0.8 mg Nalbuphine as safe intrathecal adjuvant to local anesthetic for prolongation of analgesia with fewer side effects.

The regression of sensory blockade for two segment and at S1 was prolonged in group N that was statistically significant.Hence, Nalbuphine provides prolonged duration of analgesia.Aparna Jayara et al[3] in her study observed that Nalbuphine prolongs the the duration of two-segment sensory regression and sensory regression to S1.A study conducted by B. Shraddha et al[7] in 2016 on effects of intrathecal Nalbuphine as an adjuvant for postoperative analgesia concluded that Nalbuphine prolongs the duration of sensory regression to S1 and total duration of analgesia.

The request to rescue analgesia (injection Diclofenac 75mg IV) was delayed in group N and that was statistically highly significant.The study conducted by Amar Prakash Kataria et al[1] concluded that Nalbuphine prolongs the duration of time to 1st request to rescue analgesia as compared to Ketamine. The results of this study corroborated with our study. In 2013, in the study conducted by N. Hemanth et al[6] for studying the effect of intrathecal ketamine as additive to 0.5% hyperbaric bupivacaine intrathecally, they observed ketamine to prolong the duration of analgesia with the time to request to 1st rescue analgesia being 150.8±11.7 minutes that was in contrast to our study.

Marzieh Beigom Khezri et al[8] in 2013 conducted a study to evaluate analgesic effects of Ketamine as an additive to intrathecal Bupivacaine in cesarean section and found that Ketamine provides earlier onset of motor blockade and prolonged duration of motor blockade as compared to control group.Also, there was prolongation of duration of anaesthesia and time to request first rescue analgesia was prolonged.The duration of motor blockade was lesser than that observed in our study whereas the duration of 1st request to rescue analgesic was more prolonged than that observed in our study.

In their study conducted by Amar Prakash Kataria et al[1], incidence of hypotension, bradycardia, nausea/vomiting was similar to our study.In their study side effects like shivering, headache, backache,etc were also observed that were not observed in our study.

CONCLUSION:

It was concluded from our study that Nalbuphine has earlier onset of sensory blockade and peak sensory level alongwith prolongation of time to two segment regression and regression of sensory level to S_1.There was longer duration of postoperative analgesia and so the time to first rescue analgesic requirement was prolonged in Nalbuphine group as compared to Ketamine group.There was a comparable haemodynamic stability in both the groups intraoperatively.

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