ORIGINAL RESEARCH PAPER

Anaesthesiology

THE COMPARATIVE STUDY OF IV KETAMINE VERSUS IV FENTANYL ON POST-OP ANALGESIA IN PARTURIENTS UNDERGOING CESAREAN SECTION UNDER SPINAL ANESTHESIA

KEY WORDS: Ketamine, Fentanyl, Post-operative analgesia, Intraoperative nausea and vomiting.

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ABSTRACT

Introduction: Spinal anesthesia is most commonly used anesthetic technique for cesarean section . Postoperative pain can interrupt contact between mother and newborn as it can delay early ambulation and discharge. The most commonly used intravenous opioids for postop analgesia is Fentanyl. Ketamine prevents central sensitization to pain and sub-anesthetic doses is effective in reducing analgesic requirements in the first 24 hours after surgery. **Aims:** The aim of our study is to compare the effect of intravenous low dose ketamine and fentanyl on parturient undergoing cesarean section under spinal anesthesia on the duration of postoperative analgesia and its side effects. **Materials And Methods:** This is a Randomized comparative study. It is conducted from January 2023 to July 2023 on patients undergoing caesarean section in Vani Vilas Hospital attached to Bangalore Medical College and Research Institute, Bangalore. This prospective, randomized comparative study will be performed after obtaining institutional and informed consent from the patients. These patients will be allocated into two groups randomly in which each group had 33 parturients. **Result:** The demographic parameters were comparable within both groups. In our study, the meantime for the duration of post-op analgesia was 3.3±0.5 hrs in group K and 2.8±0.6 hrs in group F, the difference of 0.5 hrs with p-value of 0.0003 which was statistically significant. Group K also had reduced pain scores and had fewer side effects compared to Group F. **Conclusion:** IV ketamine provides longer duration of post-op analgesia with fewer side effects like nausea, vomiting and shivering when compared to IV Fentanyl.

INTRODUCTION

Spinal anesthesia with hyperbaric bupivacaine is the most commonly used anesthetic technique for elective cesarean section and emergency scenarios due to its simplicity and ease of performance, low cost and quick installation of anesthesia, providing adequate analgesia and muscle relaxation for the surgery[1].

The greatest concern of mothers undergoing cesarean section is postoperative pain . When pain is not controlled appropriately, it can interrupt contact between mother and newborn and when postoperative pain is severe, it can delay early ambulation and discharge; thus, appropriate pain control after cesarean section is essential[2].

The various analgesic modalities of post-op analgesia identified were IV opioid's, Low dose ketamine, TAP block, Local anaesthetic wound infiltration, NSAIDS and acetaminophen, Intrathecal additives, Epidural analgesia[2].

The ideal post-CS analgesic regime should be efficacious without impacting the ability of mother to take care of the neonate and with minimal drug transfer through breast milk[2].

Ketamine is a non-competitive antagonist of the N-Methyl-D-aspartate receptor (NMDA-R) that inhibits central sensitization and has a preemptive analgesic effect to relieve postoperative pain[3] .Ketamine in sub-anaesthetic doses is effective in reducing analgesic requirements in the first 24 hours after surgery. Ketamine also decreases postoperative analgesic consumption due to prevention from opioids tolerance.

Despite years of advances in pain management, the mainstay of postoperative pain therapy in many settings is still opioids. Opioids bind to receptors in the central nervous system and peripheral tissues and modulate the effect of the nociceptors. The most commonly used intravenous opioids for postop is fentanyl. It is synthetic derivative of morphine - potent, shorter onset of action and half life[4].

Rationale of study: Many studies showed Ketamine and fentanyl are both used for post op analgesia but in our study we are going to observe the efficacy of ketamine as compared to fentanyl in duration of post op analgesia and reduced side effects like intra op nausea vomiting, shivering and respiratory depression.

MATERIALS AND METHODS

This randomized comparative study was carried out from January 2023 to June 2023 following approval from the Institutional Ethics Committee. The study included 66 parturients classified as American Society of Anesthesiologists (ASA) physical status II, all of whom underwent lower segment cesarean section (LSCS) under spinal anesthesia. The participants were between 18 to 35 years old and provided informed consent to participate. Exclusion criteria were Not willing to give consent, Parturients with medical and obstetric complications like anaemia, heart diseases, gestational hypertension, uncontroled gestational diabetes, shock, septicemia and hypertension, Parturients with history of hypersensitivity to local anesthetics, ketamine and fentanyl, Subjects having any absolute contraindications for spinal anaesthesia like increased ICP, severe hypovolemia, bleeding diathesis, local infection, Parturients with height < 150cm and >170 cm and BMI >30 6 and Mentally retarded parturients.

After obtaining the ethics committee clearance, Parturients of various hospitals attached to Bangalore Medical College and Research Institute fulfilling the inclusion criteria were taken in to study after obtaining written informed consent. Demographic data, History, Clinical examination, Details of investigations were recorded in the study proforma. In the preoperative examination, the patient was asked for history of systemic illness like Diabetes mellitus, Hypertension, Bronchial asthma, Seizure disorder, Hemorrhagic disorders,

Neurological disorders. History of any chronic drug intake and allergic reactions to drugs were noted.

66 Parturients were randomly allocated into two groups K and F of 33 each by a computer-generated random sequence table from www.randomization.com. Both the groups received study drug randomly after extraction which was concealed for both observer and parturient.

Data were collected in the case record proforma meeting the objectives of the study. Preoperative assessment was done for each patient and written informed consent were taken. All patients were premedicated on the night before surgery with Tablet Ranitidine 150mg, fasted 8 hours for solid food and 4 hours for clear fluids. Intravenous line were obtained with 18-gauge cannula and were preloaded with Ringer lactate 500ml half an hour before anaesthesia. All patients received Inj. Ranitidine 50mg IV and Inj. Metoclopromide 10mg IV for aspiration prophylaxis before surgery. All patients were transported to OT in left lateral position. Monitoring was done according to ASA, which included electrocardiography (ECG), non-invasive blood pressure (NIBP) and pulse oxymetry. Patients were placed in left lateral position. Under aseptic precautions lumbar puncture was performed at the level of L3- L4 interspace through a midline approach using 25 G Quincke's spinal needle and study drug was injected after confirmation of needle tip in the subarachnoid space by clear and free flow of cerebrospinal Fluid. Intrathecal injection Bupivacaine0.5% 2cc was given over approximately 10-15s.

Patients were made to lie supine immediately and then wedge below the right hip to displace the gravid uterus. The cephalad spread of sensory blockade was checked using the pinprick method at regular intervals. The motor blockade was checked using the Bromage scale. After 10 min of spinal anesthesia and achieving the required level of sensory and motor blockade. Patients were monitored with ECG, NIBP, SPO2 and respiratory rate at regular intervals. Patients were randomly divided into 2 groups namely Group K and Group F where both patients received study drug after extraction of fetus. After completion of the surgery, patients were shifted to the postoperative recovery room and observed .

Postoperative VAS score was noted at the intervals of 30 min, 60 min, 90 min, and 6 h .And in post-operative period if VAS >5 Inj paracetamol 1g iv infusion was given and monitored .The time of the 1st rescue analgesic administration was recorded and a chart was maintained. Patients were monitored 24 h postoperatively. Intraoperative shivering were assessed by Crossley and Mahajan grading. If shivering score >2 were treated with Inj Tramadol 50mg slow iv. Side effects like nausea, vomiting, pruritus, bradycardia, hypotension, respiratory depression, urinary retention etc were monitored. IV Ondansetron 4mg was used to treat nausea and vomiting. Hypotension was treated with bolus of fluid and incremented dose of Mephentermine 6mg iv.

A power analysis based on a previous study conducted by Forghani M, Esfahani MN, Vali M et al [5], the pain score after 15 minutes of intervention in group Fentanyl was 3.18+1.17 and group Ketamine was 3.32+1.90. Considering the similar mean and the variation for the present study, a sample size of 33 participants per group was calculated. Data collected was entered in MS Excel and analyzed using SPSS ver 21.0. Descriptive statistics was represented using mean SD, percentage and proportion. Association between any categorical variable with the two groups were analyzed using Chisquaretest. P Value less than 0.05 indicates that there is an association between the groups and the categorical variable. Statistically significant difference among the two groups with respect to any continuous variable were analyzed using Independent Sample T test. P value less than 0.05 indicates that there is a significant difference between the mean values among the two groups with respect to that variable.

RESULTS

The study included 66 patients, with 33 in Group K, who received Inj Midazolam 1mg iv with Inj Ketamine 0.3mg/kg iv and 33 in Group F, who received Inj Midazolam 1mg iv with Inj Fentanyl 1mcg/kg iv. There was no significant differences between the two groups in terms of demographic characteristics such as age, weight, height and BMI (Table 1). Additionally, there was no statistically significant differences between the groups with respect to heart rate and mean arterial pressure. There was statistically significant differences between the groups with respect to duration of post-op analgesia, VAs score, IONV and Shivering (Table 2 and 3)

Table 1:

PARAMETER	GROUP K(n-33) Mean ±SD	GROUP F(n-33) Mean ±SD	P-VALUE
Age (years)	26.2±4.4	27.1±4.7	0.419
Weight (kg)	65.3±5.1	62.3±5.4	0.061
Height (cm)	160.5±4.6	162.2±4.0	0.107
BMI (kg/cm^2)	25.3±2.7	23.8±1.9	0.075
Heart rate (/min)	92.7±12	93.4±10.2	0.784
MAP (mmHg)	76.6±5.6	77.0±4.0	0.707

MAP - Mean Arterial Pressure; BMI – Basal Metabolic Rate

Table 2:

	GROUP K(n-33) Mean ±SD	GROUP F(n-33) Mean ±SD	P-VALUE
Duration of post-op analgesia	3.3±0.5	2.8±0.6	0.0003
VAS score	3.67±0.48	4.85±0.87	0.0005

Table 3:

PARAMETER	GROUP K(n-33)	GROUP F(n-33)	P-VALUE
IONV	33.3%	66.7%	0.007
Shivering	36.4%	63.6%	0.027

IONV – Intraoperative Nausea And Vomiting

In our study, the duration of post Operative analgesia, was significantly higher in Group K (3.3 ± 0.5 hours) compared to Group F (2.8 ± 0.6 hours), as illustrated in Figure 1.

When comparing pain scores between the two groups using the Visual Analogue Scale (VAS) at 30, 60 and 90 minutes postoperatively—a significant difference was observed. Group K, which received Inj Midazolam1mg iv with Inj Ketamine 0.3mg/kg iv., consistently exhibited significantly lower VAS scores compared to Group F (Inj Midazolam1mg iv+Inj Fentanyl 1mcg/kg iv.). This difference was most pronounced at 90 min postoperative with a p-value of less than 0.0005, confirming the enhanced pain control provided by the addition of ketamine. (Figure 2)

Figure 1.

Figure 2.

Figure 3.

Figure 4.

Intraoperative nausea and vomiting was significantly lower in

group K (33.3%) compared to group F (66.7%) as given in Figure 3. Shivering was significantly higher in group F (63.6%) compared to group K (36.4%) as given in Figure 4.

DISCUSSION

A review article "Breastfeeding after Anesthesia: A Review for Anesthesia Providers Regarding the Transfer of Medications into Breast Milk" conducted by Cobb et al [6] concluded that breast feeding can be resumed even with administration of Midazolam ,Fentanyl, low dose ketamine and low dose morphine after cesarean section which was consistent with our study.

Frolinch et al.[7] conducted a study "A single dose of fentanyl and midazolam prior to Cesarean section have no adverse neonatal effects" on 60 parturients which showed no differences in neonatal outcome variables (Apgar score, neurobehavioural scores, continuous oxygen saturation between two groups, concluding that it improves patient's comfort without inducing adverse effects in the newborn or maternal amnesia during peripartum period.

In our study, the duration of post operative analgesia was significantly higher in Group K (3.3 ± 0.5 hours) compared to Group F (2.8 ±0.6 hours) and VAS scores were consistently lower in Group K compared to Group F at 30, 60 and 90 minutes postoperatively.

Our findings align with those of Rahmanian et al.[8], who conducted a study "The Effect of Low-Dose Intravenous Ketamine on postoperative pain following cesarean section with spinal anaesthesia- A randomised clinical trial" on 160 parturients showed the mean and standard deviation of pain scores at one, two, six and 12 hrs following surgery were 4.95±1.2, 5.38±1.06, 6.16±0.27 and 4.64±0.47 for control group and 3.55±0.31, 3.92±1.33, 3.90±1.7 and 3.19±0.67 for ketamine group with p-value of <0.001. They concluded that it reduces the need for post operative analgesics and has fewer side effects than using opioids.

A study "Comparison of the Effect of Intravenous Fentanyl with Low-Dose Ketamine on Pain Relief in Patients Taking Methadone and Suffering from Limb Fractures" conducted by Forghani et al [9] on 100 patients showed that the mean pain score of patients 15 min after the intervention was significantly lower in the low-dose ketamine group (2.50 ± 1.34) than in fentanyl group (7.10 ± 1.43) with p-value < 0.001. They concluded that low dose ketamine relieves pain with faster effect in shorter time than fentanyl after the intervention which aligned with our study.

Our findings were correlating with Shahid et al.[10], who conducted a study "The Duration Of Postoperative Analgesia Using Low Dose Intravenous Ketamine In Patients Undergoing Elective Cesarean Section With Spinal Anesthesia A Randomized Controlled Trial" on 60 parturients showed the mean duration of analgesia in group bupivacaine-ketamine and bupivacaine group were 3.85±0.98h and 1.40±0.62 h respectively with a p-value of 0.0005. They concluded that IV low-dose ketamine provides more effective and long lasting pain relief.

In our study, intraoperative nausea and vomiting was higher in Group F compared to group K. Shivering was significantly higher in group F compared to group K.

Also a study "Effect of ketamine on intraoperative nausea and vomiting during elective caesarean section under spinal anaesthesia: A placebo-controlled prospective randomized double blinded study" conducted by Shabana et al [11] on 229 patients showed that the incidence of intraoperative nausea was 20.9% in the ketamine group compared with 40.9% in the placebo group, which was statistically significant (p-value 0.004). They concluded that administration of IV ketamine in parturients posted to elective CS under spinal anaesthesia reduced the incidence of intraoperative nausea and hypotensive episodes compared to placebo group which is consistent with our study.

A study "Effect of fentanyl on nausea and vomiting in cesarean section under spinal anesthesia: a randomized controlled study" conducted Shin et al [12] on 80 parturients showed that the incidence of IONV was significantly lower in the Midazolam fentanyl group compared to Midazolam group (5% [2/40] vs. 25% [10/40]). They concluded that addition of fentanyl to midazolam was effective for sedation, analgesia and to prevent intra operative nausea and vomiting in cesarean section which was aligned with our study .

Pradeep Kumar Dash et al.[13] conducted a study "Effects of Intravenous Ketamine, Butorphanol and Fentanyl for the Management of Intraoperative Shivering under Spinal Anaesthesia- A Randomised Clinical Trial" on 90 patients showed that shivering control time was shorter in Butorphanol (3.6±1.20 min) than in Ketamine (3.867±1.676 min), but significantly longer in Fentanyl (5.467±2.047 min). Shivering recurrance was more common in Fentanyl (20%) than in Ketamine (0%) and Butorphanol (0%) group. They concluded that butorphanol is faster acting, followed by ketamine and then fentanyl to control of shivering which was consistent with our study where IV ketamine was effective in controlling shivering than IV fentanyl.

CONCLUSION

We came to the conclusion that the research on the "the comparative study of iv ketamine versus iv fentanyl on post-op analgesia in parturients undergoing cesarean section under spinal anesthesia" is iv ketamine not only provides a longer duration of post operative analgesia, but also lesser side effects of intraoperative nausea, vomiting and shivering when compared to iv fentanyl.

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