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COMPARISON OF POSTOPERATIVE ANALGESIC EFFECT OF KETAMINE AND FENTANYL ADDED TO INTRATHECAL BUPIVACAINE IN PATIENTS UNDERGOING ABDOMINAL HYSTERECTOMY: A PROSPECTIVE RANDOMIZED DOUBLE-BLIND STUDY

Anesthesiology

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ABSTRACT

Background & Aims: To compare the analgesic efficacy of ketamine and fentanyl added to intrathecal hyperbaric bupivacaine in patients undergoing elective abdominal hysterectomy.

Methods: Seventy-two patients of ASA grade I/II, 40-60 years old were recruited in a prospective double-blinded, randomized comparative study. Spinal anaesthesia was performed in group F using hyperbaric 0.5% bupivacaine 15mg combined with 25 µg fentanyl and in group K using hyperbaric 0.5% bupivacaine 15mg combined with 25 mg ketamine. The onset time and duration of sensory and motor blockade, total duration of analgesia, and the incidence of adverse effects were recorded.

Results: The onset of sensory and motor block was significantly faster in group K (2.15±0.44 min &1.24±0.44 min) as compared to group F (2.83±0.44 min & 1.81±0.46 min). Duration of sensory and motor block was longer in group F (96.97±8.20 min & 131.33±10.82min) than in group K (88.58±5.91 min & 120.69±6.61min). Mean duration of analgesia was 159.92±11.19 min and151.58±8.10min in group F and group K respectively.

Conclusion: Addition of ketamine or fentanyl to spinal bupivacaine were equally effective in pain control after abdominal hysterectomy.

KEYWORDS

INTRODUCTION

Spinal anaesthesia is the most popular and preferred technique of regional anaesthesia till date for lower abdominal surgeries. Hyperbaric bupivacaine is most commonly used local anaesthetics for spinal anaesthesia. Several intrathecal adjuncts are being used to enhance spinal anaesthesia. Currently, opioids are widely used for pain relief, but they often provide sub-optimal analgesia with occasional serious side effects. Fentanyl is the most frequently used intrathecal lipophilic opioid as analgesic adjuvant with minimal cephalad spread making it most safer of all the intrathecal opioids to cause delayed respiratory depression.[1] Neuraxial opioids allows prolonged analgesia in the postoperative period and faster recovery from spinal anaesthesia.[2]

Ketamine is an anaesthetic agent with potent analgesic properties and has been found to be effective by epidural and intrathecal routes. It acts by causing non-competitive antagonism at N methyl D aspartate (NMDA) receptors and a local anaesthetic effect.[1]

We conducted present study to compare the effect of intrathecal fentanyl 25µg added to 0.5% hyperbaric bupivacaine versus intrathecal ketamine 25 mg added to 0.5 % hyperbaric bupivacaine with respect to characteristics of sensory and motor blockade, duration of analgesia as primary outcome variable and hemodynamic variations and adverse effects as secondary outcome measures.

Material & Methods

After approval by Institutional Ethics Committee, this prospective, randomized, double-blind, comparative study was conducted in a tertiary care centre. Seventy-two patients belonging to American Society of Anaesthesiologists (ASA) I-II patients, 40 – 60 yrs. of age, undergoing elective abdominal hysterectomy under spinal anaesthesia were recruited in this study. Patient's refusal for block, presence of bleeding disorders, local infection at the site of block, any history of allergy to study drugs were excluded from study. Patients in whom spinal anaesthesia failed were also excluded from the study. All patients were explained about the procedure, advantages and risks of the procedure during the preoperative assessment done one day prior to surgery and then informed consent was obtained from the patient. The patients were randomized into two groups using chit in box method.

Group F – patients received 15 mg (3mL) hyperbaric bupivacaine 0.5% + 25 µg fentanyl intrathecally.

Group K - patients received 15 mg (3mL) hyperbaric bupivacaine 0.5% + 25 mg ketamine preservative free intrathecally.

After shifting the patient inside operation theatre, chits were opened by anaesthesiologist not involved in the study to prepare the drug solution according to randomization. The observer who collected the peri-operative data as well as the patients was blinded to the drug solution administered.

After checking the fasting status, routine standard monitoring including pulse oximeter, non-invasive blood pressure and five lead electro-cardiogram was commenced and baseline parameters, i.e., heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), peripheral oxygen saturation (Spo2) were recorded. Intravenous access was established using 18G, intravenous cannula and preloading was done with 10ml/kg of inj. Ringer's lactate solution.

Spinal anaesthesia was performed in the left lateral position using a 25-gauge spinal needle at L3-4 interspace using a midline approach. After free flow of cerebrospinal fluid, the premixed solution (3.5 mL) was injected over 30 seconds according to the group assigned. Patient was then placed supine with a 15-degree head tilt to achieve level of block up to T5-T6.

HR, SBP, DBP and SpO2 were noted at baseline, immediately after block performance and then every 2 min for the first 10 min and then at 15, 25, 40 and 60 min, followed by every 30 min till the end of the surgery. Hypotension was defined as a fall in systolic pressure >20% below baseline and injection ephedrine 5 mg IV was given. Bradycardia (heart rate <50/min) was treated with intravenous atropine sulphate 0.02 mg/kg.

The level of sensory block was assessed every minute by pinprick in the dermatomes T-10, T-8 and T-6, until a stable level of block was achieved at T6 level. Thereafter assessment was done at 15 min interval till one hr and then at 30 minutes interval till the patients complained of pain. Time of onset of sensory blockade was taken as the time to attain the highest level of sensory blockade. Two segment regression time was defined as time of regression of sensory level by two segments from the highest level attained. The duration of sensory block was defined as the time from intrathecal injection to regression of the sensory block to L1.

Motor block was assessed using Bromage score [0 = no motor block; 1

= inability to raise extended leg, able to move knees and feet; 2 = inability to raise extended leg and move knee; able to move feet; 3 = complete motor block of limb]. The onset of motor blockade was taken as the time taken to achieve Bromage grade 3 blocks from the time of intrathecal injection. Duration of motor block was defined as the time elapsed from the Bromage score 3 to 0.

The duration of analgesia was defined as the time from spinal injection to the time of administration of first rescue analgesic for pain in the postoperative period. Postoperatively, intramuscular diclofenac 75 mg was given for rescue analgesia, whenever the pain score was >3. It was considered as the end point of the study.

The incidence of side effects such as hypotension, bradycardia, pruritus, nausea and vomiting were noted every 15 min during surgery and 2, 4, 8, 12 h postoperatively.

The primary outcome variable included block characteristics and duration of analgesia. The secondary outcome variable was haemodynamic changes and adverse effects.

Perioperative monitoring of heart rate and noninvasive blood pressure was done every 2 min for the first 10 min and then at 15, 25, 40 and 60 min, followed by every 30 min till the end of the surgery and any changes greater than 20 % from the baseline value were treated.

Statistical analysis

All the data was entered in excel sheet and analyzed statistically using SPSS version XVII Quantitative data were summarized in form of mean ± standard deviation and difference in mean of two groups was analyzed using unpaired t-test. Qualitative data were summarized in form of proportion and the difference in proportion was analyzed using chi-square test. The level of significance was kept at 95% and P value of <0.05 was considered statistically significant.

RESULTS

Demographic variables were comparable between both the groups. (Table 1)

Onset of sensory block was significantly faster in ketamine group as compared to fentanyl group. (p-value<0.001). Time to achieve the highest level of sensory block was found similar in the two groups. (p-value >0.05) There was early regression to L1 dermatome in ketamine group as compared to fentanyl group (88.58±5.91 min and 96.97±8.20min respectively), it was highly significant statistically.

Onset of motor block was significantly faster in ketamine group (1.24±0.44 min) as compared to fentanyl group (1.81±0.46 min), it was highly significant statistically (p-value<0.001). Degree of motor block was comparable in both groups as all patients showed Bromage score 3. Duration of motor block was significantly longer in fentanyl group as compared to ketamine group. (p-value <0.001)

Duration of analgesia was significantly longer in group fentanyl as compared to group ketamine. (p-value (0.01) Block characteristics are shown in table 2.

No significant difference was reported in perioperative and postoperative adverse effects like hypotension, bradycardia, shivering and nausea between both the group.

Table 1: Demographic variables

Variable	Group F (mean±SD)	Group K (mean±SD)	P-value
Number of patients in each group (n)	36	36	
ASA grade I/II	7/29	12/24	
Age in Yrs.	38.67 ±5.70	39.39±7.01	>0.05
Duration of surgery	80.58±11.77	77.58±7.07	>0.05

Group F-Fentanyl; Group K-Ketamine; S.D-Standard deviation

Table 2: Characteristics of block

Variable	Group F (mean±SD)	Group K (mean±SD)	P-value
Onset of sensory block (min)	2.83±0.44	2.15±0.44	<0.001 (HS)
Onset of motor block (min)	1.81±0.46	1.24±0.44	<0.001(HS)
Duration of sensory block (min)	96.97±8.20	88.58±5.91	<0.001(HS)
Duration of motor block (min)	131.33±10.82	120.69±6.61	<0.001(HS)
Total duration of analgesia (min)	159.92±11.19	151.58±8.10	<0.01(HS)

Group F-Fentanyl; Group K-Ketamine; S.D-Standard deviation

Table 3: Incidences of adverse effects

Adverse effect	Group F	Group K	P-value
Hypotension	9 (25%)	8 (22.22%)	>0.05 (NS)
Bradycardia	5 (13.88%)	4 (11.11%)	>.0.05 (NS)
Shivering	2 (5.56%)	2(5.56%)	>0.05 (NS)
Nausea	4 (11.11%)	4 (11.11%)	>0.05 (NS)

Group F-Fentanyl; Group K-Ketamine

DISCUSSION

In present study, we observed that addition of preservative free ketamine to intrathecal hyperbaric bupivacaine led to faster onset of both sensory and motor blockade, although it did not prolong the duration of spinal analgesia compared to addition of fentanyl to intrathecal hyperbaric bupivacaine in patients scheduled for abdominal hysterectomy under spinal anaesthesia. Our results are in accordance to other studies [3,4,5,6]. Reason for it may be attributed to the axonal conduction block produced by the ketamine.[7]

The median Bromage score were similar in both the groups. These observations are similar to other studies.[8]

Duration of sensory-motor block and postoperative analgesia was found to be longer in fentanyl group in comparison to ketamine group, similar observations were made in studies done by Unlugenc et al[4] Shrestha et al[9] and Kathirvel et al[6]. While, Galindo et al[10] found longer duration of analgesia with ketamine, they suggested that the decrease in pH of local anesthetics on addition of ketamine produced a more rapid onset and longer duration of blockade, a finding contrary with our finding. Togal et al[11] also observed similar findings. However, the discrepancy of the results may be due to different methodologies.

Hypotension remained the most commonly observed adverse effect, but it was manageable with fluid bolus or with inj atropine. Incidence of hypotension observed more in fentanyl group in comparison to ketamine group. Similar observations made in other studies [6,12,13]. Bion[13] suggested that the transmission of ketamine into the venous system (azygos vein) of the spinal cord leads to hemodynamic stability during spinal anesthesia.

CONCLUSION

Addition of preservative free ketamine 25 mg to 15 mg of hyperbaric bupivacaine 0.5% led to faster onset of both sensory and motor blockade, although it did not prolong the duration of spinal analgesia compared to addition of fentanyl 25 µg to 10 mg of hyperbaric bupivacaine 0.5% undergoing abdominal hysterectomy with spinal anaesthesia. Fentanyl provides prolonged duration of analgesia. So, we conclude that both ketamine and fentanyl are equally effective adjuvant to intrathecal bupivacaine.

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