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COMPARISON OF EFFICACY OF INTRATHECAL FENTANYL AND KETAMINE AS AN ADJUVANT TO BUPIVACAINE IN TOTAL ABDOMINAL HYSTERECTOMY.

Anesthesiology

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ABSTRACT

BACKGROUND: Spinal anesthesia with bupivacaine has been the most preferred mode of anaesthesia for lower abdominal surgeries owing to its inherent advantages. Various adjuvants like fentanyl and ketamine are used with local anaesthetic agents in spinal anaesthesia to improve quality of anaesthesia, prolong postoperative analgesia, and decrease side effects.

AIM The purpose of this study was to compare the efficacy, onset and duration of sensory and motor block , degree of postoperative analgesia and possible side effects of intrathecal bupivacaine (0.5%) with ketamine and intrathecal bupivacaine (0.5%) with fentanyl in patients scheduled for total abdominal hysterectomy.

MATERIALS AND METHODS: This prospective, randomized double blind, study included 72 ASA class I and II patients undergoing total abdominal hysterectomy under spinal anaesthesia. The patients were randomly divided in two groups of 36 each using a chit in box method.: Group BF (bupivacaine fentanyl group): 3 ml of 0.5% hyperbaric bupivacaine and 25 µg fentanyl. Group BK (bupivacaine ketamine group): 3 ml of 0.5% hyperbaric bupivacaine and 25 mg ketamine.

RESULTS: The onset of sensory block was earlier in group BK as compared to group BF. Mean time of onset of motor block in group BF was 1.81 + 0.46 minutes and for group BK was 1.24+ 0.44. The duration of sensory block and postoperative analgesia was longer in Group BF. The mean duration of motor block was 131.33 ± 10.82 minutes in group BF and 120.69 ± 6.61 minutes in group BK. Itraoperative adverse effects were not significant in both the groups.

CONCLUSIONS: Addition of ketamine leads to rapid onset of both sensory and motor blockade whereas addition of fentanyl prolongs the duration of sensory blockade providing longer period of analgesia

KEYWORDS

Bupivacaine, Fentanyl, Spinal Anaesthesia, Ketamine , Abdominal Hysterectomy

Introduction

Spinal anesthesia with bupivacaine has been the most preferred mode of anaesthesia for lower abdominal and lower limb surgeries. The subarachnoid block has got inherent advantages like intense motor and sensory blockade, good relaxation, reliability, avoids side effects of multiple drugs used in general anaesthesia, no post operative respiratory depression, nausea vomiting and drowsiness. It also has good patient and surgeons acceptability and decreases the hospital stay. It can also be administered safely in many patients with systemic diseases where general anaesthesia and endotracheal intubation can be hazardous, like sensitive airway diseases, hepatic and renal diseases, endocrine disorders and cardio vascular diseases.

Bupivacaine has been the gold standard drug for the safe conduct of spinal anaesthesia [1]. Discovery of various spinal receptors like α2-adrenergic, cholinergic, opioid, NMDA, GABA, benzodiazepam receptors triggered the usage of drugs like eclonidine,[2] neostigmine,[3] opioids,[4] ketamine,[5] midazolam [6] for synergistic effect with hyperbaric bupivacaine (0.5%) in prolonging the effect of anaesthesia.

However, concerns have been raised in the past few years regarding (1) the safety of this drug as bupivacaine is more cardiotoxic (2) its prolonged effects may lead to a delay in motor block resolution, urinary retention and a prolonged hospital stay. These problems limit the use of bupivacaine in day-care settings. Alternatively, agents with a short effect such as lignocaine are associated with transient neurological symptoms. Various adjuvants have been used with local anaesthetic agents in spinal anaesthesia in order to improve quality of anaesthesia and decrease their side effects. Lipophilic opioids (e.g.-fentanyl and sufentanyl) and ketamine are increasingly being administered intrathecally as adjuvants to local anaesthetics.[7,8]

As there are not many studies comparing efficacy of intrathecal bupivacaine (0.5%) with ketamine and intrathecal bupivacaine (0.5%) with fentanyl, we decided to compare these two drugs in our present study and assess their efficacy and compare the onset and duration of sensory and motor block and also the degree of postoperative analgesia and possible side effects.

Method

In this prospective and double blind randomized controlled study, 72 female patients, between 40-60 years of age, of height more than 145cm, ASA Grade I and II who were scheduled for total abdominal hysterectomy were selected.

After obtaining approval from the institutional ethics committee and ascertaining selection criteria, informed, valid written consent was obtained from each of the patients for participation in the study. Exclusion criteria were: Patients refusal, patients on chronic analgesic therapy, with gross spinal deformity, with peripheral neuropathy, taking sympathomimetics or sympatholytic drugs, known allergy to local anesthetics, history of chronic headache or backache, local infection at the site and coagulation disorder.

Preoperative evaluation was carried out in all patients with detailed history and general physical examination. Vital parameters (pulse, blood pressure, oxygen saturation in room air, and respiratory rate) were noted . The patients were randomly divided in two groups of 36 each using a chit in box method.:

Group BF (bupivacaine fentanyl group): 3 ml of 0.5% hyperbaric bupivacaine and 25 µg fentanyl

Group BK (bupivacaine ketamine group): 3 ml of 0.5% hyperbaric bupivacaine and 25 mg ketamine.

The total volume of solution in both the groups was 3.5 ml.
Adequate fasting was confirmed on arrival of patient in Operation Theater. Routine monitoring ECG, non invasive blood pressure, and pulse oxymeter were attached. A peripheral venous access was secured on upper limb with 18 gauge cannula and preloading with lactated Ringer's solution was initiated at the rate of 10 ml/kg, 15 min prior to subarachnoid block. Subarachnoid blockade was performed in sitting position with midline approach with strict aseptic precautions using 25 G Quincke needle. The drug combination was prepared by a different anesthesiologist. The anesthesiologist performing the block and later monitoring the patient was blinded to the nature of drug

combination being injected intrathecally. Patients were immediately placed in supine position with 15 degree head down tilt to achieve level of T5-T6 block. Oxygen face mask was applied with flow rates 6 L/min.

Definitions and parameter studied

1. Hypotension was defined as a mean arterial blood pressure (MABP) < 70 mmHg and treated by incremental doses of ephedrine 5 mg IV until the correction of Systolic arterial blood pressure.
2. Bradycardia was defined as fall in heart rate below 55 beats per min and treated with incremental doses of atropine 0.5 mg IV.
3. Respiratory depression was defined as a respiratory rate less than 8 breaths/min and/or oxygen saturation less than 90% in room air.
4. Onset of sensory block was defined as the time from the intrathecal injec-tion of the study drug to the time taken to achieve the T-10 level of sensory block. This was assessed by pin-prick test bilaterally at the mid-clavicular line by using 25 G needle. The highest level of the block and the time to achieve the same was also noted.
5. Duration of sensory block was defined as the time from intrathecal injection to the time taken to regression of sensory block upto L1 dermatome
6. Onset of motor block was defined as the time from the intrathecal injection of the study drug to the time taken to achieve the highest degree of motor block.Degree of motor block was assessed by using Bromage score

Score	Criteria
0	Full movement
1	Inability to raise extended leg, can bend knee
2	Inability to bend knee, can flex ankle
3	No movement

7. Duration of motor block was defined as the time from intrathecal injection to the time taken to regression of motor block to Bromage score 0.
8. Duration of complete motor block was defined as the time from intrathecal injection to the time taken to regression of the block to a Bromage score of <3.
9. Duration of analgesia was defined as the time from the intrathecal injection to the first request of analgesic.
10. Adverse effects like hypotension, bradycardia, pruritus, nausea and vomiting were noted.
11. Patient's first demand for rescue analgesia constituted the end point of the study.

Results

In present study no statistically significant difference was found in mean age , height,duration of surgery and ASA grade between the two groups. (Table-1)

Mean time of onset of sensory block in group BF was 2,83 + 0.44 minutes, and for group BK was 2.15+ 0.44(Table-2). There was highly significant difference ($p < 0.001$) in time of onset of sensory block between the two groups. It was earlier in group BK as compare to group BF. Mean time of onset of motor block in group BF was 1.81 + 0.46 minutes and for group BK was 1.24+ 0.44. (Table-3). There was highly significant difference ($p < 0.01$) in time of onset of motor block between the two groups. Onset of motor block was earlier in group BK.

Table 4 shows the mean duration of sensory block. It was 96.97 ± 8.20 minutes in group BF and 88.58 ± 5.91 minutes in group BK. There was highly significant difference ($p < 0.01$) noted in the duration of sensory block between the groups showing longer duration of sensory block in Group BF.

Mean duration of motor block was 131.33 ± 10.82 minutes in group BF and 120.69 ± 6.61 minutes in group BK. (Table-5). There was highly significant difference ($p < 0.01$) noted in the duration of motor block between the groups showing longer duration in BF Group. There was no significant difference ($p > 0.05$) in intra-operative adverse effects like hypotension, bradycardia, shivering and nausea between the two groups. (Table-6).

Table – 1 Demographic profile of study population

Parameter	Group BF	Group BK
Number of patients	36	36
Mean age (in years)	37.80±6.21	38.27 ±5.78
Mean height (in years)	155.74 ± 3.76	154.26 ± 3.91
ASA grade I/II	7/29	12/24
Duration of surgery (in minutes	79.84 ± 9.43	82.33± 7.84

Table-2 Onset of sensory block

T10 level sensory block (in minutes)	Group BF		Group BK	
	No	%	No	%
1.5-2.5	7	19.44	25	69.44
2.5-3.5	28	77.78	11	30.58
3.5-4.5	1	2.78	0	0.00
Total	36	100.00	36	100.00
Mean ±SD	2.83 ±0.44		2.15±0.44	
p-value	<.001			

Table-3 Onset of motor block

Onset of motor block (in minutes)	Group BF		Group BK	
	No	%	No	%
1-2	8	22.22	28	77.78
2-3	27	75.00	8	22.22
3-4	1	2.78	0	0.00
Total	36	100.00	36	100.00
Mean ±SD	1.81 ±0.46		1.24 ±0.44	
p-value	<.001			

Table-4 Duration of sensory block

Duration of block (in minutes)	Group BF		Group BK	
	No	%	No	%
75-84	4	11.11	11	30.56
85-94	8	22.22	21	58.33
95-104	15	41.67	4	11.11
105+	9	25	0	0.00
Total	36	100.00	36	100.00
Mean ±SD	96.97 ±8.20		88.58 ±5.91	
p-value	<.001			

Table-5 Duration of motor block

Duration of block (in minutes)	Group BF		Group BK	
	No	%	No	%
105-114	1	2.78	6	16.67
115-124	9	25.00	21	58.33
125-134	13	36.11	8	22.22
135-144	9	25.00	1	2.78
145+	4	11.11	0	0.00
Total	36	100.00	36	100.00
Mean ±SD	131.33 ±10.82		120.69 ±6.61	
p-value	<.001			

Table 6- Intra-operative adverse effects

Adverse effect	Group BF		Group BK		p-value
	No	%	No	%	
Hypotension	9	25	8	22.22	>.05
Bradycardia	5	13.88	4	11.11	>.05
Shivering	2	5.56	2	5.56	>.05
Nausea	4	11.11	4	11.11	>.05

Discussion

Subarachnoid block with bupivacaine has been most extensively used mode for lower abdominal surgery[9] because of its reliability, and longer duration of action in comparison to lignocaine.

Fentanyl, a highly lipophilic opioid, has rapid onset of action following intrathecal administration.[10] Opioid receptors were identified in central neurosystem in 1971 and were found to be precisely located in the posterior horn of spinal cord. [11,12] Effectiveness of intrathecal opiods depends on degree of ionization and lipophilicity of the drug.

Bion [13] first used spinal ketamine for victims of war surgery in a human beings. Spinal ketamine binds to the phencyclidine site of the NMDA receptor-gated calcium channel and inhibits the NMDA receptors noncompetitively. [14]

In present study early onset of sensory block was found in group BK while the duration of sensory block was found longer in Group BF. Our results are comparable with study conducted by with Ashok Shankar et al [15] in regards with effects of Intrathecal Ketamine added to Bupivacaine for Spinal anaesthesia which showed trends towards earlier onset of both sensory and motor blockade in the ketamine

group. Similarly Unlugenc et al [16] also observed that addition of ketamine with hyperbaric bupivacaine resulted into early onset and shorter duration of sensory blockade in comparison to adding fentanyl with bupivacaine

In present study early onset of sensory block as found group BK. Our findings were consistent with the study carried out by D Bhattacharya et al[17] who studied the clinical effects of intrathecal hyperbaric bupivacaine and ketamine and observed that ketamine had early onset of sensory block.

In present study we observed that addition of fentanyl prolongs the duration of sensory block and reduce the analgesic requirement in the early postoperative period following spinal anaesthesia. Our results coincided with the study conducted by Singh H et al [18]

In our study we found that intrathecal ketamine administration with a low dose of bupivacaine resulted in early onset and shorter duration of sensory block. Our results were comparable with the study conducted by Togal T et al [19] who reported that Intrathecal ketamine administration with a low dose of bupivacaine provides shorter motor and sensory block onset time, shorter duration of action and less motor blockade in elderly males

In present study early onset of motor block was found in group BK but the duration of motor blockade was longer in group BF. However no significant difference in the degree of motor block was found between the two groups. Our results coincides with results of study conducted by Kathirvel S et al[5] who concluded that onset of motor block was earlier in patient who had received ketamine and duration of motor block was longer in the patients who had received opioid. Similarly our results coincided with the study conducted by Unlugenc et al [16] and Togal T et al [19]

In present study addition of ketamine with bupivacaine led to rapid onset of both sensory and motor blockade and enhanced the segmental spread of spinal block. Our results coincided with the study conducted by Gunasty et al [20] who found that addition of ketamine to ropivacaine led to rapid onset of both sensory and motor blockade and enhanced the segmental spread of spinal block.

The quality of Intraoperative analgesia was quite good in all patients. No patient of any group complained of discomfort on skin incision. There was significant ($p < 0.05$) difference in mean duration of analgesia between two groups showing longer duration of analgesia in group BF. Our results coincide with studies conducted by Unlugenc et al [16] and Singh H et al [18] who also observed that addition of ketamine to bupivacaine as compared to fentanyl has less duration of analgesia postoperatively. Our results also coincides with the study conducted by Biswas et al [21] who also demonstrated that adding of fentanyl with hyperbaric 0.5% bupivacaine markedly prolongs post operative analgesia and significantly reduces the requirement of postoperative analgesic

Hypotension was the most frequent adverse effect in both groups intraoperatively. This hypotension was easily treated by incremental dose of ephedrine without any sequels. Hypotension was observed in little higher number of patients in bupivacaine fentanyl group, in contrast to bupivacaine ketamine group. But this difference was not significant. Other adverse effect like shivering, nausea, and bradycardia were also observed in few patients but it was not significant.

Conclusion

It was concluded that addition of ketamine with bupivacaine provided faster onset of sensory and motor blockade, and rapid recovery from motor blockade and hemodynamic stability such as lower incidence of hypotension and bradycardia which is beneficial for early ambulization. Addition of fentanyl with bupivacaine provided longer duration of sensory and motor blockade and longer duration of analgesia which is beneficial in post operative period.

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