Original Research Article

Comparative study between ketamine and bupivacaine intrathecally in lower abdomen and lower limb surgery

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Abstract

Background: There is an on-going quest to know which agent is the better agent for intrathecal anaesthesia for pain relief due to surgical stimuli. Bupivacaine is commonly used local anaesthetic agent for spinal anaesthesia but it has some disadvantages like slower onset of action. Ketamine shows beside its general anaesthetic effect, a local anaesthetic like action. Series of studies have shown a potent analgesia after spinal administration of ketamine alone or in combination with opioids and α_2 agonists, suggesting that ketamine alters pain perception at the spinal level. So, the objective of this study to compare the effectiveness of Ketamine action intrathecally with that of bupivacaine in respect to onset & duration of analgesia, onset & duration of motor block, sedation, cardiovascular effects and any other side effects like nausea, vomiting.

Materials and methods: In this hospital based prospective comparative study, 100 patients of ASA (American Society of Anaesthesia) I and II scheduled for lower abdominal and lower limb surgery were taken. Patients were divided into two equal groups. **Group I** – Received 3 ml of hyperbaric bupivacaine (0.5%). **Group II** – Received 3 ml of hyperbaric Ketamine [taken from 2ml of preservative free ketamine (100mg) added with 2ml of 5% dextrose]. Onset and duration of analgesia, onset and duration of motor block, central effects like sedation, effects on cardiovascular system and any other side effects were compared in both the groups. Analysis data was carried out using the available statistical package of SPSS-20 (Statistical Package for Social Science – version 20 "PASW" statistics).

Results: The onset of sensory block and motor block were faster in ketamine group as compared to bupivacaine group. The duration of analgesia was longer in ketamine group as compared to

bupivacaine group. The duration of motor block was almost equal in both the groups. About sedation, more patients were sedated in ketamine group as compared to bupivacaine group. Patients in ketamine group were more stable cardiovascularly as compared to bupivacaine group.

Conclusion: Ketamine can be used as a pure local anaesthetic for spinal anaesthesia with advantage of faster onset of analgesia and motor block as well as longer duration of analgesia. Ketamine group appeared more hemodynamically stable also. So, ketamine can be used as an alternative to bupivacaine for moderate duration of lower abdomen and lower limb surgery despite its central effect like sedation.

Key words

Intrathecal anaesthesia, Bupivacaine, Ketamine, Lower limb surgery, Lower abdominal surgery.

Introduction

In man's struggle to survive, perhaps his greatest and indeed his constant battle are against pain. General anaesthesia and central neuraxial block are two discoveries for relief of pain due to surgical stimuli. In developing countries like ours spinal analgesia is the most common technique because it is economical and more commonly used in remote areas where anaesthetic gas supply is not available.

Spinal anaesthesia is used extensively for lower abdominal and lower extremity surgeries because it has many advantages over general anaesthesia like minimal physiological disturbance, minimal intraoperative blood loss, optimal operative conditions, less chance of pulmonary aspiration in patients with full stomach.

Bupivacaine is the most commonly used local anaesthetic agent for spinal anaesthesia but it has some disadvantage like slow onset of action, it causes profound hypotension, and bradycardia, may be risky in uncorrected hypovolemia patients. Further research lead to discovery of spinal opioid receptors. Many opioids and non-opioids were tried intrathecally for both intraoperative and postoperative analgesia. The opioids have definitely certain complications like respiratory depression, nausea, vomiting, retention of urine, itching etc, although they may provide postoperative analgesia like local anesthetics. Further research on the field of pain perception and treatment led to the discovery of non opioid spinal pathways mediating analgesia. Search for other alternatives found potent analgesic effect after spinal administration of ketamine alone or in combination with opioid and α_2 agonists in both animals and humans, suggesting that ketamine alters pain perception at spinal level [1].

Ketamine, a phencyclidine derivative acts on variety receptors including opioid receptors, N-methyl-D-aspartate receptors (NMDA) complex channel, blocks peripheral and central nervous system Na+ channels and voltage gated K+ and Ca++ channel which are of eminent importance for suppressing pain transmission in peripheral nerves, dorsal root ganglion neurons and dorsal horn neurons of spinal cord [2, 3]. It is found to be effective by intrathecal and epidural route. It possesses some advantages over the conventional local anaesthetic agents as it does not depress cardiovascular system [4, 5]. The onset of anaesthesia (sensory block) and motor paralysis is found to be earlier than the conventional local anaesthesia [5]. Intensity of sensory block is 100% as it is described to be due to potent analgesic effect of ketamine [6]. Incidence of nausea, vomiting, headache, disturbance of micturition is less with this agent [8].

The objective of this study was to compare effectiveness of ketamine action intrathecally with that of bupivacaine in respect to onset and duration of analgesia, onset and duration of motor block, sedation, cardiovascular stability and any other side effects.

Materials and methods

In this hospital based prospective, comparative study, 100 patients were taken. Approval from institutional ethical committee was taken. The procedure of spinal anaesthesia and the purpose of the study were explained and an informed valid consent was taken from the patient in the language they can understand.

Patient selection

100 patient of either sex, aged 25-60 years of ASA I and II were selected from the cases posted for routine lower limb and lower abdomen surgery, from different surgical units of the hospital (orthopaedics, general surgery, obstetrics and gynaecology).

Patient refusal, contraindication to regional blockade like local skin sepsis, patient with bleeding disorder, ASA III and IV, deformed back, uncooperative patient, allergy to any of used drugs and patient with psychological disorder were excluded from the study.

Preoperative examination

During the preoperative visit, detailed history of every patient was noted and complete physical examination and necessary investigations were done.

Anaesthesia technique

100 patients were divided randomly into 2 groups of 50 each.

Group I - received 3ml of hyperbaric bupivacaine (0.5%)

Group II - received 3ml of hyperbaric ketamine [3ml taken from 2 ml of preservative free ketamine (100 mg) + 2ml of 5% dextrose]

Spinal anaesthesia was carried out by standard technique. It was carried out under strict aseptic condition with 25 G spinal needle through L3-L4 intervertebral space in sitting position and patients were immediately place in supine position.

Arterial blood pressure, pulse rate and respiratory rate were measured every 5 minutes till the sensation returned to normal. Supplementation of oxygen 3L/min was given to all patients through a facemask. I.V fluid was given as per requirement.

Following parameters were studied

- Onset of sensory block (analgesia) - assessed by pin prick method.
- Duration of sensory block (analgesia) - was calculated from the time of administration of drug to the time of first request for systemic analgesia.
- Onset of motor blockade was assessed by straight leg raising test while lying supine.
- Duration of motor blockade was calculated from time of onset of action to the reappearance of movements.
- Central effects like sedation-as sedated or awake (sedated- state of reduced consciousness in which verbal contact with the patient can be maintained).
- Effects on cardiovascular system – By measuring pulse rate and systolic blood pressure in every 5 minutes till sensation returned to normal.
- For other side effects like nausea, vomiting, headache, restlessness, allergic reaction and urinary retention. Patients were observed before and at 1, 2, 5, 10, 20, 30 minutes after injection, during operation & also in the post-operative period.

Statistical analysis

Analysis data was carried out using the available statistical package of SPSS-20 (Statistical Package for Social Science – version 20 "PASW" statistics).

Data was presented in simple measures of percentage, mean and standard deviation. The significance of difference of different means (quantitative data) was tested using independent student-t test, while different percentages (qualitative data) were tested using Pearson Chi-square test, statistical significance was considered whenever the P value was less than 0.05.

Results

The onset of sensory block assessed by pin prick in group I was 2-6 minutes with a mean of 3.5 ± 0.02 (SE) as compared to 1-3 minutes with a mean of 1.5 ± 0.05 (SE) In group II. It was observed that onset of analgesia was quicker in ketamine group as compared to bupivacaine group. It was statistically significant (P<0.001) (**Table - 1**).

Table - 1: Onset of sensory block.

	Group I	Group II
Range (in minutes)	2 - 6 min	1 - 3 min
Mean ± SE	3.5 ± 0.02	1.5 ± 0.05
'P' value	**P < 0.001 Significant**	

The duration of analgesia determined by from time of administration of drug to the time of first request for systemic analgesia in group I was 120 to 140 minutes with a mean of 132 ± 0.20 (SE) as compared to 140 – 160 minutes with a mean of 155 ± 0.30 in group II. It was statistically significant. It was observed that duration of analgesia was more in ketamine group as compared to bupivacaine group (P<0.001) (**Table - 2**).

Table - 2: Duration of Sensory Block.

	Group I	Group II
Range (in minutes)	120 - 140	140 - 160
Mean ± SE	132 ± 0.20	155 ± 0.30
'P' value	**P < 0.001 Significant**	

Considering the mean value, it was observed that onset of motor paralysis was quicker in group II (i.e. 2.5 ± 0.05) compared to group I (5.5 ± 0.15) which was significant (P<0.001) (**Table - 3**). Considering the mean value, it was observed that the duration of motor paralysis is nearly equivalent in both the groups (P<0.004) (**Table - 4**).

Table - 3: Onset of Motor Block.

	Group I	Group II
Range (in minutes)	3 - 9	2 - 4
Mean ± SE	5.5 ± 0.15	2.5 ± 0.05
'P' value	**P < 0.001 Significant**	

Table - 4: Duration of Motor Block.

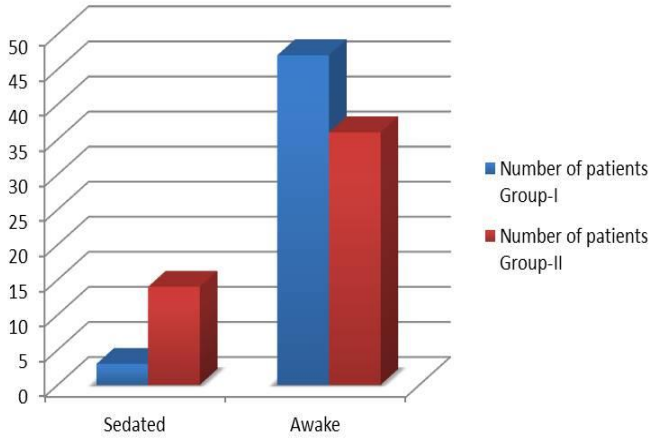
	Group I	Group II
Range (in minutes)	95 - 145	90 - 140
Mean ± SE	116 ± 0.1	123 ± 1.2
'P' value	**P < 0.004 Significant**	

Twenty eight percent of patient received ketamine intrathecally were sedated as compared to six percent of patient were sedated on bupivacaine group, which is statistically significant (P<0.001) (**Table - 5**, **Graph - 1**).

Table - 5: Central Effects (Sedation).

Sedation	Group I		Group II	
	No. of patients	%	No. of patients	%
Sedated	3	6%	14	28%
Awake	47	94%	36	72%
'P' Value	**P < 0.001**			

Graph – 1: Central Effects (Sedation).



In group I, 12 patients had mild hypotension while 21 patients had moderate hypotension, 5 patients had severe hypotension and 14 patients had no significant change in systolic blood pressure with a mean of 17.00 ± 1.0. In group II, 15 patients had mild hypotension and 35 patients had no significant fall in systolic blood pressure with a mean of 10.05 ± 0.50. The comparison in both groups was statistically significant. (P<0.001) (**Table - 6**, **Graph - 2**).

In group I, 32 patients had no significant change in pulse rate while 13 patients had mild change in

pulse rate and 5 patient had moderate change in pulse rate in comparison to 42 patients had no significant change in pulse rate while 8 patients had mild change in pulse rate in group II, which was significant (P< 0.001) (**Table - 7**, **Graph - 3**).

As for other adverse effects like nausea, vomiting, headache, urinary retention, we did not get any patient having all these side effects except one having nausea and vomiting in ketamine group, so there was no significant difference between the two groups.

Table - 6: Change in Systolic Blood Pressure.

Change in Systolic Blood Pressure	**Group I**		**Group II**	
	Number of patients	**%**	**Number of patients**	**%**
Not Significant	14	28	35	70
Mild (10-20 mmHg)	12	24	15	30
Moderate (21-30 mmHg)	21	42	0	0
Severe (>30 mmHg)	5	10	0	0
Mean ± SE	17.00 ± 1.02		10.05 ± 0.50	
'P' value	**P < 0.001 Significant**			

Graph – 2: Change in systolic blood pressure in mm of Hg.

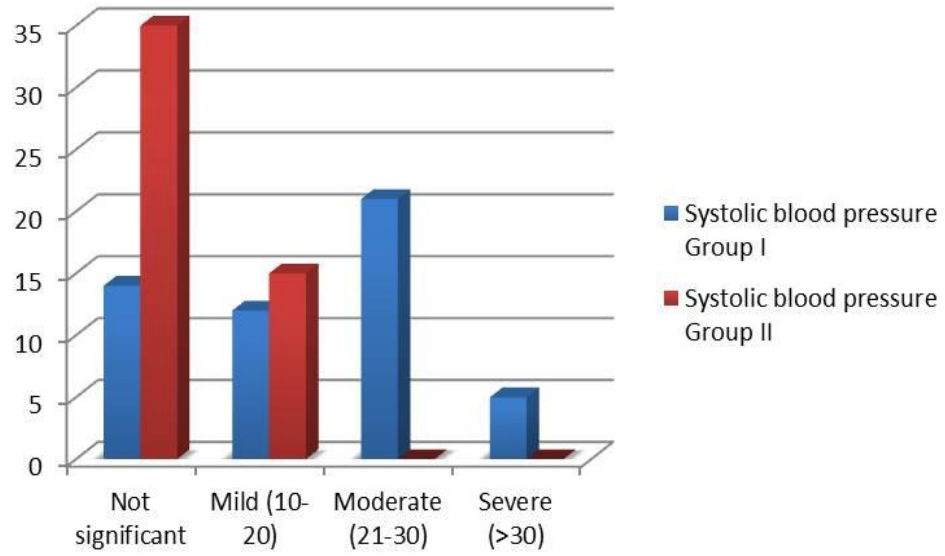
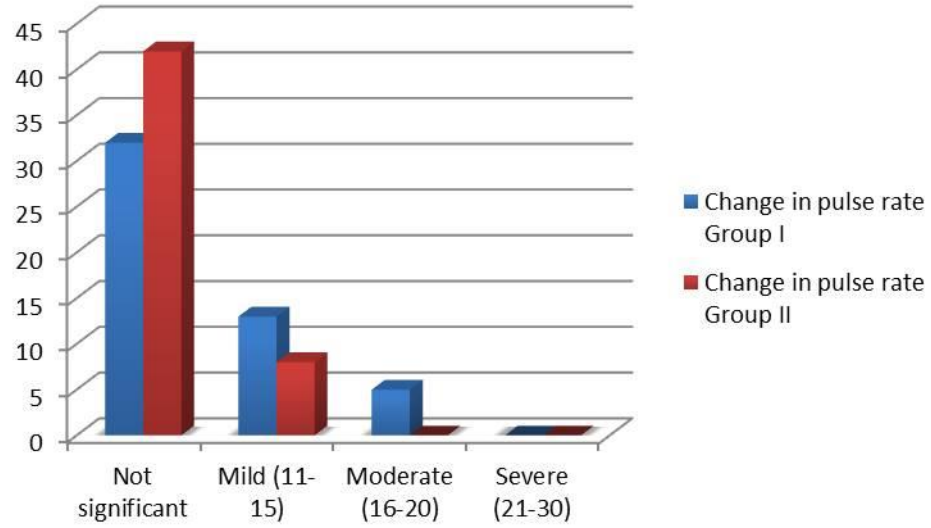


Table - 7: Changes in Pulse Rate.

Change in Pulse Rate	**Group I**		**Group II**	
	Number of patients	**%**	**Number of patients**	**%**
Not Significant	32	64%	42	84%
Mild (11-15 bpm)	13	26%	8	16%
Moderate (16-20 bpm)	5	10%	Nil	Nil
Severe (21-30 bpm)	Nil	Nil	Nil	Nil
Mean ± SE	9 ± 0.80		19 ± 2.00	
'P' value	**P < 0.001 Significant**			

Graph – 3: Change of pulse rate in bpm.



Discussion

The popularity of spinal anaesthesia is ever increasing day by day, because of its unique advantages over general anaesthesia. The commonly used local anaesthesia bupivacaine has its own disadvantages. So, there is an ongoing quest for better agent for intrathecal anaesthesia. Ketamine, a phencyclidine derivative is a potent analgesic [7] because of its modest affinity for opioid receptors and non-competitive NMDA (N- methyl D- Aspartate) receptor antagonism. It blocks peripheral and central nervous system sodium channels and voltage gated potassium and calcium channels which are of eminent importance for suppressing pain transmission in peripheral nerves, dorsal root ganglion neurons and dorsal horn neurons of spinal cords. So, it seemed worthwhile to investigate the possibility of exploiting the potent analgesic property of ketamine by its intrathecal administration.

The onset of sensory block was between 1 – 3 minutes in group II compared to 2 – 6 minutes in group I, which was significant ($P < 0.001$). The duration of sensory block was 140 – 160 minutes in group II while it was 120 – 140 minutes in group I, which again was significant ($P < 0.001$). The faster onset of (analgesia) sensory block assessed by pinprick method in group II as compared to group I come in agree with study of Dipasri Bhattacharya and Arnab Banerjee [8]. The duration of sensory block which was calculated as from the time of administrating the drug to the time of first request for systemic analgesia was longer in ketamine group as compared to bupivacaine group which also came in agree with Dipasri Bhattacharya and Arnab Banerjee [8] where they had calculated this as postoperative analgesia. Analgesia provided by ketamine was more prolonged; this can be explained by the other shared mechanism of the drug other than blocking Na++ channels such as NMDA receptor antagonism [9] and Mu opioid receptor agonism.

The onset of motor block determined by loss of movements of the lower limbs in group I was 3 – 9 minutes with a mean of 5.5 ± 0.15 (SE) as compared to 2 – 4 minutes with a mean of 2.5 ± 0.05 (SE) in group II. The duration of motor block determined by the regaining of motor power and joint movement was 94 – 145 minutes with a mean of 116 ± 0.1 in group I as compared to 90 – 140 minutes with a mean of 123 ± 1.2 in group II and the difference was significant ($P < 0.004$). So, the onset of motor loss was found to be earlier in case of intrathecal Ketamine as compared to intrathecal bupivacaine and the duration of motor block was found to be almost equal in both the groups. So, our study was in

agree with Bansal SK, Bhatia VK study [5] where they had found that intrathecal Ketamine has faster onset of action.

In our study, 28% of patients received ketamine intrathecally were sedated as compared to 6% of patients were sedated in bupivacaine group, which is statistically significant. This may be due to systemic effect resulting from intravascular absorption of ketamine [10, 11]. In the study done by Dipasri Bhattacharya and Arnab Banerjee [8] where they had found all the patients receiving intrathecal ketamine showed moderate degree of sedation which indicated that ketamine has some central effects. In that study in bupivacaine group many patients were drowsy which may be because of premedication (Diazepam) used in that study. So, they concluded that intrathecal Ketamine has some central effect like sedation. We also noticed the same thing in our study. Bansal, et al. (1994) found that sedation was observed with all the doses used in his study, which was of mild or moderate intensity with the patients being easily arousable from the sleep [5].

In our study, we found that maximum number of patients showing no significant change in pulse rate by intrathecal Ketamine. In bupivacaine group more patients having mild as well as moderate fall in pulse rate as compared to Ketamine group. Maximum number of patients showing no significant change in systolic blood pressure by intrathecal Ketamine in comparison to intrathecal bupivacaine where patients showing hypotension. In Kalyani Govindan, et al. [12] study, it was found that the patients given ketamine intrathecally were hemodynamically more stable, we also noticed the same thing in our study.

As for other adverse effects like nausea, vomiting, rigor, headache and urinary retention there was no significant difference between the two groups. Only one patient showed nausea and vomiting in Ketamine group may be because of surgical pathology or manipulation of abdominal viscera. In study done by Kaliyani Govindan, et al. [12] on 60 patients scheduled for lower abdominal and lower extremities surgeries under spinal anaesthesia, divided into four groups given spinal anaesthesia by different doses (75 mg or 100 mg), Ketamine alone or in combination with epinephrine, 86% of the patients had nystagmus (no patients had nystagmus in our study), two had vomiting (one reported in our study) and one patient had delirium (not reported in our study) that needed to be treated with IV Diazepam. They claim that these side effects may be due to systemic absorption of the drug or migration of ketamine via the CSF to the lateral ventricle. Surgical pathology or manipulation of abdominal viscera which may be the cause of nausea and vomiting. The cause of higher percentage of nystagmus and appearance of delirium in one patient may be the use of higher doses of ketamine.

Conclusion

As a new look to an old drug, Ketamine can be used as a pure local anaesthetic for spinal anaesthesia with the advantage of faster onset of sensory and motor block, longer duration of analgesia, minimal changes is mean blood pressure and pulse rate as compared to bupivacaine. But it is having drawback of central effect like sedation. Despite its central effect intrathecal ketamine could be a good alternative to intrathecal bupivacaine especially in lower limb and lower abdomen surgery.

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