A COMPARATIVE STUDY OF KETAMINE (HEAVY) WITH 5% LIGNOCAINE (HEAVY) INTRATHECALLY FOR CAESAREAN SECTION- A RANDOMISED CONTROL TRIAL

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ABSTRACT

BACKGROUND

Spinal anaesthesia for caesarean section has gained popularity since it decreases the complications of general anaesthesia. High incidence of spinal hypotension, neonatal bradycardia and decreases in neurobehavioral scores are not uncommon with the use of 5% Lignocaine.

The aim is to evaluate the efficiency and safety of Ketamine as a sole anaesthetic agent and compare it with 5% Lignocaine in spinal anaesthesia.

MATERIALS AND METHODS

This randomised control trial is conducted among 100 pregnant females belonging to ASA I and I-E in the age 25-35 years, weighing 41-75 kg and height of 140-165 cm. Group 1 (n=50) patients received 50 mg of 5% lignocaine intrathecally. Group 2 (n=50) patients received 75 mg of Preservative-free ketamine HCL in 25% Dextrose intrathecally. Onset of sensory blockade, maximum spread & duration of analgesia, onset & duration of motor blockade, APGAR score at 1 & 5 min. are compared. Intraoperative hypotension, bradycardia and other side effects are noted.

RESULTS

Onset of sensory block in group 1 is faster than group 2 ($p < 0.001$). Maximum spread and duration of analgesia was statistically insignificant between two groups. Onset of motor block in group 1 is faster than group 2 ($p < 0.05$). Duration of motor block and APGAR at 1& 5 min. was statistically significant between two groups. Intraoperative hypotension is more common in group 1 than group 2.

CONCLUSION

Intrathecal ketamine provides good analgesia, duration of analgesia and motor blockade obtained is good and adequate for caesarean section. So ketamine is a safe and effective anaesthetic agent and it can be tried safely in emergency caesarean section.

KEYWORDS

Subarachnoid Block, Motor Block, Sensory Block, APGAR Score.

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BACKGROUND

Spinal anaesthesia for caesarean section has gained popularity since it decreases the complications of general anaesthesia like acid aspiration syndrome, hypoxia associated with difficulty in tracheal intubation laryngospasm, overdose of anaesthetics, chronic hypoventilation which all result in maternal and foetal mortality and morbidity. However, high incidence of spinal hypotension has been reported in up to 92% of cases with the use of 5% Lignocaine. Neonatal bradycardia and decreases in neurobehavioral scores are known to occur in mothers whose systolic blood pressure decreases more than 30% of the baseline levels.[1]

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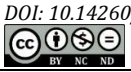

Local anaesthetics are usually injected in acid solution as hydrochloride salt. Following injection, the pH increases as a result of buffering in the tissues and a proportion of the drug dissociates to release free base which is determined by pKa of the solution.[2]

As it is lipid soluble, the free base is able to pass through the lipid cell membrane to the interior of the axon, where re-ionisation takes place. The re-ionised portion enters the sodium channels and simply plugs the channel so that sodium ions cannot enter the cell. As a result, no action potential is generated or transmitted and conduction blockade occurs.

Lignocaine is amide local anaesthetic with moderate potency and duration, but of good penetrative powers and rapid onset of action. It acts directly on nerves causes loss of vasomotor tone, sensation and motor power. It stabilises the cell membrane of cardiac tissue. It depresses the automaticity in abnormal or damaged fibres. Initially, lignocaine causes anxiety, restlessness and drowsiness. With moderate toxicity, it causes numbness of tongue, circumoral paraesthesia and twitching. Severe toxicity causes convulsions. Respiratory and cardiac depression is due to medullary depression.

It is quickly absorbed from the intrathecal space, mucosal surfaces and after parenteral administration. The duration of action of lignocaine is 45 minutes to 1 hour and with

adrenaline 1.5 to 2 hours. Maximum dose is 3 mg/kg (200 mg) without adrenaline and 7 mg/kg (500 mg) with adrenaline.[3]

Ketamine is a non-barbiturate and non-narcotic agent.[4] It belongs to phencyclidine group of drugs. It increases both uterine tone and the intensity of uterine contractions.[5] It increases uterine blood flow without adversely affecting foetal cardiovascular and acid base status. It crosses the placental barrier but there is no foetal depression. Ketamine has an oxytocic effect (Gallon 1971); this is useful in operation for the removal of the retained products of pregnancy and elective abortion, but it is contraindicated in first and second trimesters of pregnancy.[6,7] It causes a selective sensory blockade of cortical association areas and thalamo-cortical projection system, without depressing the reticular activating system and limbic system.[8,9,10]

Proposed Mechanism of Action of Ketamine as a Spinal Anaesthetic[11,12]

1. Ketamine may bind to opiate receptors as an agonist.
2. Ketamine may act as an NMDA receptor antagonist.
3. Ketamine may have local anaesthetic like effect when used intrathecally.

Aim of the Study

1. To evaluate the efficiency and safety of Ketamine as a sole anaesthetic agent for Caesarean section in spinal anaesthesia.
2. To compare the effects of Ketamine with 5% Lignocaine in spinal anaesthesia.

MATERIALS AND METHODS

This randomised control trial was conducted at the Government Theni Medical College Hospital, Theni. Patients were randomly divided into two groups using randomly permuted blocks and an online software (http://www.randomization.com).

A total of 100 pregnant females in the age 20-35 years, weighing 41-75 kg, of the height 140 – 165 cm were randomly selected for this study. All the patients belonged to ASA physical status I and I-E. All patients with systemic disorders were excluded. Informed consent was obtained from all the 100 patients after a detailed explanation of the procedure to be done.

Basic data like pulse rate, blood pressure, respiratory rate, haemoglobin estimation, urine analysis for albumin and sugar blood urea, sugar and serum creatinine, X-ray chest and electrocardiogram were taken if required. All the patients were explained about the procedure. Postoperative followup and the postoperative questionnaire regarding pain and consent was obtained from them. Patients were not premedicated to avoid any possible interference with the outcome of study.

Preservative-free Ketamine hydrochloride (Aneket, Neon Laboratories Pvt. Ltd.) 50 mg/mL solution used for spinal analgesia. As it was found to be hypobaric (Specific gravity 0.9488), hyperbaric solution was prepared using the addition of 25% Dextrose for study group patients.[13]

Specific gravity and pH for Lignocaine - 1.020 & 7.
Specific gravity and pH for ketamine - 1.025 & 6.5.

Inside the operation theatre, once again the pulse rate, blood pressure were recorded. The patients were cannulated with 18 G IV cannula and preloaded with lactated Ringer's solution. The patients were randomly divided into two groups of 50 each. The lumbar puncture was performed in right lateral position with 24 G spinal needle, at the level of L3 – L4 interspace under aseptic precautions.

Group 1 (n=50) patients received 50 mg of 5% lignocaine intrathecally.

Group 2 (n=50) patients received 75 mg of preservative-free ketamine HCL in 25% Dextrose intrathecally.

After the subarachnoid injection, patients were put in supine position and with left lateral tilt provided by a wedge under right buttock.[14] Oxygen 5 L/minute was administered through face mask. When the sensory blockade reached, T6 level surgery was started. The effect of anaesthetic agents was observed on the following parameters.

Analgesia

It was subjectively studied by pinprick method with a sterile 24 G needle. The patient was rested initially every 30 seconds until the maximum level was stationary. After 30 minutes it was tested once in 5 minutes to assess recovery. The time taken for the onset of analgesia and total duration of analgesia assessed by two segment regression time were noted.

Motor Blockade

This was tested and graded according to Bromage scale which states as given below.

Grade 1	100%	Complete	Unable to Move Feet or Knee
Grade 2	66%	Almost complete	Able to move only feet
Grade 3	33%	Partial	Able to move the knees
Grade 4	0%	Null	Complete flexion and extension of knees and feet

Evaluation of Cardiovascular Stability

The systolic blood pressure and pulse rate were recorded every minute for the first 10 minutes, then every 5 minutes until the operation was over. All the patients were infused with injection oxytocin 10 units in 540 mL of 5% Dextrose solution after the delivery of the baby.

Hypotension was defined as a decrease in systolic blood pressure of 30% or more from the baseline recording and was promptly treated with intravenous Ephedrine hydrochloride 6 mg increments, in addition to rushing of IV fluid.[15,16] If the pulse rate falls below 60/minute, injection atropine sulphate 0.5 mg IV was given.

The incidence of hypotension and the dose of ephedrine required to correct it were noted in both groups. The APGAR score of neonate was calculated at 1 and 5 minutes. The occurrence of side effects during the procedure like nausea, vomiting, shivering, bradycardia, difficulty in breathing, delirium and hallucinations were noted.

Statistical analysis; Data were entered into Microsoft Excel Worksheet 2010 and analysed using Epi Info 7 statistical software. Descriptive data were interpreted using Tables. Unpaired T test was used to compare between Group 1 and Group 2. Significance level was fixed at 95% CI (Confidence interval) for P value < 0.05.

RESULTS

	Group 1	Group 2
Age (Year) Mean	20-35 24.46	20-35 24.5
Height (cm) Mean	140-168 154	140-164 152
Weight (kg) Mean	45-65 48.04	40-65 50.32
Table 1		

Of the 100 patients, 50 patients belonged to Group 1 (5% Lignocaine 50 mg) and other 50 patients belonged to Group 2 (75 mg Ketamine). Age, weight, height were not significantly different and was comparable between two groups.

	Group 1	Group 2	P value
Onset of Sensory block			
Range (in sec.)	0-120	0-125	< 0.001
Mean ± SD	42.7 ± 29.9	76.08 ± 30.7	
Duration of Analgesia			
Range (min.)	30-60	25-65	>0.1
Mean ± SD	43.8 ± 8.95	5.7 ± 9.21	
Table 2			

Sensory Block

Onset of Sensory Blockade

The mean time of onset of analgesia was 42.7 ± 29.9 sec. in group 1 and 76.08 ± 30.7 in group 2. They were statistically significant (t= 5.87 P <0.001) as shown in the table.

Maximum Spread of Analgesia

The maximum level of analgesia is as shown by the table.

Level of Blockade	Group 1	Group 2
T4	11	6
T6	39	44
Total	**50**	**50**
Table 3		

Duration of Analgesia

Duration of analgesia assessed by the two segment regression time.

Two segment regression time is the time taken for the level of analgesia to regress by two segments from the maximum level.

The range was 30 – 60 min. and a mean of 43.8 ± 8.95 min. in group 1. The range was 25-65 min. and a mean of 45.7 ± 9.21 min. in group 2. P value is >0.1. This was also statistically not significant.

	Group 1	Group 2	P value
Motor Block onset			
Range (in sec)	60-120	60-138	<0.05
Mean ± SD	100.1 ± 37.1	151 ± 51.3	
Duration of Motor blockade			
Range (in min.)	40-75	45-80	>0.1
Mean ± SD	55.4 ± 12.04	58 ± 11.48	
APGAR Score			
1 min.	9.7058 ± 1.88	9.62574 ± 1.90	>0.5
5 min.	9.7843	9.7843	
Table 4			

Motor Block

Onset of Motor Blockade

The time taken for onset of motor blockade was a mean of 100.1 ± 3.71 sec. in Group 1 and a mean of 151 ± 51.3 sec. in group 2. P value is <0.05. It was statistically significant.

Total Duration of Motor Blockade

It is the time taken from initial onset until complete recovery of motor blockade. It is statistically not significant as shown in table 3.

APGAR score at 1 min. and 5 min.: It is comparable in both groups and is statistically not significant.

Intraoperative Cardiovascular Changes

Pulse Rate

There was increase in pulse rate from second minute onwards in both the groups and it comes to the baseline value in study group at 8th minute and 6th minute in control group and it was statistically significant at 5th and 6th minute (p<0.05).

Blood Pressure

Systolic blood pressure decrease of more than 30% below the pre-anaesthetic value was taken as hypotension and it was treated with nasal oxygen, IV fluids and inj. Ephedrine. Fall in BP was noticed at 2nd minute in control group and 3rd minute in study group. The difference is nearly 20 mmHg of systolic blood pressure. The incidence of hypotension was more in lignocaine group. The average amount of ephedrine required to treat these patients are also high. In group 1, 23 patients had hypotension and they required 6 mg of ephedrine each. In group 2, 5 patients had hypotension and they required about 6 mg of ephedrine each. This is statistically significant. (P <0.001).

Per-operative Complications

The side effects in both the groups are mentioned below-

Side Effects	Group 1	Group 2
Bradycardia	1	-
Nausea and vomiting	2	3
Table 5		

The postoperative period was uneventful in both the groups.

DISCUSSION

Bion 1984 used ketamine to produce surgical anaesthesia by injecting it intrathecally for war injuries and found no interference with cardiovascular or respiratory functions. Bion used 5-50 mg of ketamine with 5% Dextrose. The mean onset time was about 76.08 seconds and duration was 45-90 minutes. Our studies showed that mean onset time was about 76.08 seconds and duration was 58 minutes with 75 mg of ketamine. In his patients, analgesia outlasted the motor weakness which is correlating.

S. K. Bansal et al 1994 evaluated intrathecal ketamine for emergency war surgeries in 50 mg, 75 mg and 100 mg dosage schedules. With 75 mg they were able to obtain sensory loss for 41 minutes and motor loss for 47 minutes whereas our average values were 45.7 minutes and 58 minutes.

Bion S.K., Bansal et al observed mild sedative effect in all the patients. The same was observed in our patients. The

height of analgesia was seen to increase with increase in volume while levels up to T8 and T6 were obtained with 75 mg of ketamine in 25% Dextrose.

DH Lambert and BGM Caovino (1987) studied the effect of baricity of local anaesthetic solution on the level of anaesthesia. They have concluded that hyperbaric local anaesthetics produce thoracic levels of anaesthesia, owing to the gravitation of the solution to the thoracic curvature causing a high lumbar or thoracic level of anaesthesia.

Post et al (1985) state that glucose in hyperbaric solutions may delay the absorption of the drug by spinal cord. With the use of hyperbaric solution on ketamine in all our patients, we were able to obtain levels up to T6. The sedation noticed was due to systemic absorption of the drug or due to the circulation of the drug via CSF into lateral ventricles.

Dr. Devapriya Galgali has shown that intravenous ketamine of 1.5 mg/kg followed by bolus doses as sole anaesthetic in cesarean section has good analgesia, protects respiratory system reflexes, stimulate cardiovascular system and produced no bradycardia, bradypnoea or vomiting in 200 cases.

In our study, in control group, one patient had bradycardia and two patients had vomiting. In study group, there was no bradycardia but three patients had vomiting.

Spinal anaesthesia in pregnant patients has higher incidence of hypotension due to supine hypotension syndrome.

Cask RB et al 1976 studies show there was 80.92% of hypotension. This may lead to nausea, vomiting feeling unwell and even maternal death. The uterine blood flow decreases leading to foetal bradycardia, acidosis abnormal APGAR and neurobehavioural scores when maternal systolic blood pressure drops more than 30% of baseline for more than 4 minutes (Courke BC et al 1982).

Various methods have been used to prevent hypotension. Volume loading was considered a method of preventing hypotension. However, incidence of hypotension was still 60-70% in recent studies (Wout et al, 1992).

Ephedrine has been widely used as vasopressor. But it stimulates both alpha and beta receptor to increase cardiac output, heart rate, systolic and diastolic arterial pressure. The incidence of hypotension decreased to one fourth by the use of prophylactic ephedrine 1 M in a study.

In addition, large bolus doses may cause hypertension (Datta S et al 1982). In our study, the use of ketamine as sole anaesthetic has reduced the incidence of hypotension to 10% compared to control group 46%.

The requirement of ephedrine is significantly reduced to 6 mg each for 5 patients in study group and 6 mg each for 23 patients in control group. There is no neurobehavioural alterations in ketamine group. The neonatal outcome were comparable in both groups.

Fall in blood pressure was noticed at second minute in control group and third minute in study group. The difference in nearly 20 mmHg of systolic blood pressure between these two groups, is statistically significant from first minute to tenth minute. Fall in pulse rate was seen at 8th minute in control group and 6th minute in study group, and it was statistically significant at fifth and sixth minute (P. <0.05).

In this study, the pulse rate, blood pressure were well maintained which coincides with Ivankowich study 1974 which reported that cardiovascular stability is well maintained with intrathecal ketamine.

CONCLUSION

The study confirms that intrathecal Ketamine is

- A safe and effective anaesthetic agent in caesarean section.
- It provides stable haemodynamic conditions in caesarean section.
- It reduces intraoperative sedation requirements.
- Its analgesic effect extends into the postoperative period.
- The quality and duration of analgesia and motor blockade obtained is good and adequate for caesarean section.
- It can be tried safely in emergency situations.
- Hence, it is concluded that ketamine is a better newer armamentarium for subarachnoid block in caesarean section.

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