COMPARATIVE STUDY USING LOW-DOSE KETAMINE OR ONDANSETRON FOR PREVENTION OF POSTOPERATIVE SHIVERING IN PATIENTS UNDERGOING ELECTIVE CAESAREAN SECTION UNDER SPINAL ANAESTHESIA

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ABSTRACT

BACKGROUND

Post-anaesthetic shivering is of major concern, because it is one of the very important causes of patient discomfort after anaesthesia. In addition, it is also responsible for increased blood pressure, increased consumption of oxygen by the body and increased nausea and vomiting.

The aim of this study is to compare the effects of ketamine and ondansetron for prevention of shivering after cesarean section under spinal anaesthesia.

MATERIALS AND METHODS

This randomised single blind comparative clinical study was conducted on 160 pregnant patients belonging to ASA grade I presenting for elective caesarean section under spinal anaesthesia at our hospital. The patients were randomly divided into two groups of 80 each belonging to either ketamine or ondansetron groups. The ketamine group received 0.25 mg/kg of ketamine and ondansetron group received 4 mg of ondansetron. From the time of arrival of patients to recovery room to 30 minutes later, evaluation of shivering and sedation was done in addition to recording of vital signs and enquiry regarding nausea, vomiting and delusions. Comparison of quantitative variables was done using unpaired T-test and comparison of qualitative variables was done using Chi-square test.

RESULTS

Post-anaesthesia shivering was observed in 5% of patients in the ketamine group compared to 32.5% in the ondansetron group, the result being highly significant with a P value of <0.01. There was also significant difference between the two groups in terms of hypotension and sedation (P value <0.01), but no significant difference with respect to delusions (P value of 0.4969).

CONCLUSION

Ketamine in the dose of 0.25 mg/kg given intravenously caused decreased shivering compared to ondansetron in the dose of 4 mg in ASA I patients undergoing caesarean section under spinal anaesthesia.

KEYWORDS

Ondansetron, Ketamine, Post-Anaesthesia Shivering, Spinal Anaesthesia, Elective Cesarean Section.

HOW TO CITE THIS ARTICLE: Bhat MT, Hegde BK. Comparative study using low-dose ketamine or ondansetron for prevention of postoperative shivering in patients undergoing elective caesarean section under spinal anaesthesia. J. Evid. Based Med. Healthc. 2017; 4(73), 4355-4358. DOI: 10.18410/jebmh/2017/867

BACKGROUND

Shivering has been defined as involuntary movement of one or more muscle occurring at the first stage after general anaesthesia.[1] It is one of the most common problems associated with recovery from general anaesthesia.[2] Shivering occurs with both neuraxial (epidural and spinal anaesthesia) and general anaesthesia with an incidence of 40%-60% in those receiving regional anaesthesia[3] compared to 60% in those receiving general anaesthesia.[4] Post-anaesthesia shivering enhances the body's requirement for oxygen up to 500% along with increase in cardiac output, which can result in increased myocardial oxygen requirements thereby predisposing to ischaemia. Resulting hypoxia may cause lactic acidosis in older patients.[5-9] Shivering occurs in 50-65% of patients during recovery from general anaesthesia and about 30% of patients receiving local anaesthesia. Shivering can also interfere with the monitoring of oxygen saturation, noninvasive blood pressure and electrocardiogram.

Many drugs have been used for prevention of post-anaesthetic shivering, which include opioids, α2-agonists, anticholinergics, CNS stimulants and corticosteroids.[10] Ketamine is a competitive antagonist of NMDA receptor, which has been demonstrated to have an inhibitory effect on post-anaesthetic shivering.[11,12] Different doses of ketamine have been used to study its role in prevention of post-anaesthetic shivering, which include 0.5 mg/kg and

Financial or Other, Competing Interest: None.
Submission 16-08-2017, Peer Review 23-08-2017,
Acceptance 06-09-2017, Published 11-09-2017.
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DOI: 10.18410/jebmh/2017/867

0.75 mg/kg,[12,13] all of which can result in adverse effects, most notably hallucinations. Ondansetron, a 5-TH3 receptor antagonist is a commonly used drug used for prevention of postoperative and pregnancy-induced nausea and vomiting. Different studies have established the role of ondansetron in the prevention of post-anaesthetic shivering.[14,15] The present study compared the effects of a low dose of ketamine (0.25 mg/kg) with ondansetron (4 mg) for prevention of shivering after cesarean section under spinal anaesthesia in ASA I patients.

MATERIALS AND METHODS

After obtaining institutional ethics committee approval and informed written consent from patients, this prospective, randomised study was performed. One hundred and sixty patients in the age group of 20-30 years, weighing 50-60 kg and belonging to American Society of Anaesthesiologists (ASA) grade I posted for elective lower segment caesarean section under spinal anaesthesia were included and randomly allocated into two equal groups, 80 in each group. Group I received ketamine 0.25 mg/kg and group II received 4 mg of ondansetron intravenously. Patients with known contraindications to spinal anaesthesia, those with comorbidities, cardiovascular disease, mental illness, seizures, glaucoma, allergy to ketamine or ondansetron and those with obstetric complications were excluded from this study.

Pre-anaesthetic examination was carried out the previous day and all the patients were asked to fast overnight. They were premedicated with Tab. Ranitidine 150 mg p.o. the previous night and 2 hours before surgery. Monitors were attached, which included ECG, pulse oximetry and noninvasive blood pressure. Spinal anaesthesia was then performed in the left lateral position with a 25-gauge Quincke type needle using midline approach at L4-5 interspace. Once free flow of Cerebrospinal Fluid (CSF) was seen, 10 mg of 0.5% hyperbaric bupivacaine hydrochloride was injected intrathecally over 15 seconds after which supine position was assumed and left uterine tilt was given. Height of the block was tested by pinprick method using a blunt needle. Surgery was commenced when a sensory block up to T5 dermatome was reached. Body warming techniques and warm fluid therapy were not used during the surgery. The operation theatre temperature was maintained between 25-28 degrees Celsius throughout the surgery. After birth, 10 units of oxytocin was administered to patients of both the groups.

After confirming the level of block, ketamine group received 0.25 mg/kg of ketamine, which was diluted with normal saline, so as to make it to 10 mL of the solution given intravenously. Ondansetron group received 4 mg of ondansetron diluted with normal saline, so as to make it to 10 mL of the solution given intravenously. All patients received oxygen by facemask at 5 L/min. Noninvasive blood pressure was recorded every 5 minutes throughout the surgery and monitoring of arterial oxygen saturation and Electrocardiogram (ECG) was done continuously throughout the period of surgery. Systolic blood pressure less than 90 mmHg or less than 30 mmHg from the baseline was defined as hypotension and was promptly treated with intravenous fluids and intravenous bolus dose of 6 mg of mephentermine. Heart rate less than 60 beats per minute was labelled as maternal bradycardia and was treated with intravenous bolus dose of 0.6 mg atropine.

After shifting of patients to the recovery room, patients were monitored by trained nursing staff who were not aware of the classification of shivering. Shivering was graded from 0-4 using a scale similar to that shown by Tsai and Chu.[16] 0 meaning no shivering, 1 meaning no visible muscle activity, 2 meaning muscular activity in one muscle group, 2 meaning moderate muscular activity in more than one muscle group, but no generalised shaking and 4 meaning violent muscular activity that involves the whole body. In patients who had shivering of grade 3 and above in spite of having received one of the study drugs, then in such patients shivering was considered significant and was treated with tramadol 1 mg kg^{-1} IV as a rescue drug.

Sedation was graded from 1-5, 1 meaning fully awake and oriented, 2 meaning drowsy, 3 meaning eyes closed and arousable on command, 4 meaning eyes closed and arousable to physical stimuli, 5 meaning eyes closed and unarousable to physical stimuli.

In the recovery room, monitoring of blood pressure and heart rate was done every 10 minutes and enquiry about dizziness, nausea, vomiting and delusion was done. Patients were also checked for any signs of allergic reaction. They were discharged from the recovery room after the sensory level of blockade reached T10 dermatome (checked with a blunt needle at the level of umbilicus). Comparison of quantitative variables such as blood pressure and heart rate was done using unpaired T-test and comparison of qualitative variables was done using Chi-square test. Statistical analysis was done by SPSS software version 20. P-value of less than 0.05 was considered significant and P value of less than 0.01 was considered highly significant.

RESULTS

One hundred and sixty patients in the age group of 20-30 years weighing 50-60 kg and belonging to American Society of Anaesthesiologists (ASA) grade I posted for elective lower segment caesarean section under spinal anaesthesia were included and randomly allocated into two equal groups, 80 in each group. Age, height and weight were comparable in the two groups. No significant difference was detected in maternal demographic data between the two groups (Table 1). Sensory block was T5 in all the patients in both the groups. From the recovery room arrival time to 30 minutes later, evaluation of shivering and sedation was done in addition to recording of vital signs and enquiry about nausea, vomiting and delusions.

Post-anaesthesia shivering was observed in 5% patients in the ketamine group compared to 32.5% patients in the ondansetron group (Table 2). None of the patients in the ondansetron group had nausea or vomiting,

whereas 7 patients (8.75%) in the ketamine group complained of nausea and vomiting, the result being statistically significant with a P value of 0.01. All the patients in the ketamine group had sedation compared to none in the ondansetron group, the result being statistically significant with a 'P' value of less than 0.01. 2 patients (2.5%) in the ketamine group had delusions compared to none in the ondansetron group, the results not being statistically significant with a 'P' value of 0.496 (Table 3).

	Ketamine Group	Ondansetron Group	P value
Age in years (mean ± SD)	24.58 ± 2.91	24.49 ± 3.02	0.8480
Weight in kgs (mean ± SD)	55.21 ± 2.96	55.44 ± 2.92	0.6125
Height in cms (mean ± SD)	155.31 ± 2.87	155.24 ±2.77	0.8787
Duration of surgery (mean ± SD)	52.14 ± 4.24	51.68 ± 3.93	0.4777
Duration of anaesthesia (mean ± SD)	73.11 ± 4.10	72.51 ± 4.25	0.3649

Table 1. Comparison of Patient Characteristics

Shivering	Ketamine Group		Ondansetron Group		P value
	Number	Percent	Number	Percent	0.000083
Yes	4	5	26	32.5	
No	76	95	54	67.5	

Table 2. Distribution of Shivering After Surgery in the Two Groups

Complications	Ketamine		Ondansetron		P value
	Percent	Number	Percent	Number	
Hypotension	8.75	7	37.5	30	<0.05
Nausea and vomiting	8.75	7	0	0	0.0136
Sedation	100	80	0	0	<0.01
Delusions	2.5	2	0	0	0.496

Table 3. Comparison of Other Complications

DISCUSSION

Post-anaesthetic shivering is of major concern, because it is one of the very important causes of patient discomfort after anaesthesia. In addition, it can also cause increased blood pressure, increased oxygen consumption by the body and increased nausea and vomiting. The present study compared the effects of a low dose of ketamine (0.25 mg/kg) with ondansetron (4 mg) for prevention of shivering after caesarean section under spinal anaesthesia.

In our study, only 5% of patients in the ketamine group had shivering compared to 32.5% in the ondansetron group. Of the patients in the ketamine group who had shivering, only one patient had grade 1 shivering and remaining 3 patients had grade 2 shivering. Shivering controlling mechanism of ketamine has been attributed to its role on hypothalamus resulting in thermogenesis.[17] In the ondansetron group, 8 patients had grade 1 shivering, 10 patients had grade 2 shivering and 8 patients had grade 3 shivering.

Dal et al found ketamine in the dose of 0.5 mg/kg administered about 20 minutes before the end of surgery under general anaesthesia to be effective for prevention of postoperative shivering.[7] Shakya and colleagues conducted a study, which indicated that both low-dose ketamine (0.25 mg/kg) and ondansetron in the dose of 4 mg to be effective compared to saline control group for prevention of shivering during spinal anaesthesia.[3] This study by Shakya et al also showed that ketamine in the dose of 0.25 mg/kg was more effective than ondansetron in the dose of 4 mg for the prevention of shivering, which compares well with our study, which also found ketamine to be more effective than ondansetron for prevention of shivering under spinal anaesthesia.

In addition to the post-anaesthesia shivering, patients were evaluated for presence of hypotension, nausea and vomiting, delusions and sedation. Hypotension was significantly lower in the ketamine group compared to ondansetron group, the result being statistically significant with a P value of less than 0.01. Only 7 patients in the ketamine group (8.75%) had hypotension that needed to be treated with mephentermine compared to 30 patients (37.5%) in the ondansetron group who needed to be treated with mephentermine. Lesser incidence of hypotension in the ketamine group could be due to its sympathomimetic action. Our results regarding hypotension compares well with the study by Shakya et al,[3] who also found lesser incidence of hypotension in the ketamine group compared to ondansetron group.

None of the patients in the ondansetron group had nausea or vomiting compared to 7 patients in the ketamine group who complained of nausea or vomiting, the difference being statistically significant with a 'P' value of 0.01. 2 patients in the ketamine group had delusions compared to none in the ondansetron group, result not being significant with a 'P' value of 0.496. All patients in the ketamine group had different degrees of sedation compared to none in the ondansetron group, the result being statistically significant with a 'P' value of less than 0.01.

Sagir and colleagues[6] observed higher degrees of sedation after using 0.5 mg/kg^{-1} of ketamine. But, most of the patients in our study had milder degrees of sedation compared to higher degrees of sedation seen in Sagir et al study. This mild sedation circumvents the need for

supplementing any other sedative or anxiolytic medication during surgery. Quite significantly, none of the patients in our study in the ketamine group had hallucinations. Milder degree of sedation as also absence of hallucinations seen in our study may be because of the low dose of 0.25 mg/kg used in our study compared to higher dose used by Sagir et al and some other studies.

One of the limitation in our study is that we have not used a control group, which if used could have helped us in deriving better results.

CONCLUSION

Our study indicates that use of low-dose ketamine (0.25 mg/kg) is more effective than ondansetron in the dose of 4 mg for prevention of post-anaesthetic shivering during spinal anaesthesia for caesarean section in ASA I patients without causing significant adverse effects.

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