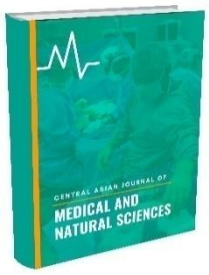
CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES



Volume: 04 Issue: 02 | Mar-Apr 2023 ISSN: 2660-4159

http://cajmns.centralasianstudies.org

Different Doses of Ketamine in Preventing Chills in Pregnant Lady with Caesarean Section Under Spinal Anesthesia

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Received 11th Feb 2023,
Accepted 10th Mar 2023,
Online 11th Apr 2023

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Abstract: Aim of the study:

To compare the efficacy and safety of ketamine 0.25 mg/kg versus ketamine 0.5 mg/kg in the prevention of chills in patients undergoing caesarean section.

design: a prospective, randomized, double-blind, placebo-controlled study. In AL sader teaching hospital Mesaan .Iraq, and AL zahraa teaching hospital / Alnajaf alashraf.

patients: 120 pregnant women 1 and 2 in ASA body status who underwent cesarean section during spinal anesthesia.

procedures

Measurements: Patient characteristics, anesthesia and surgical details, 1 and 5 minute Apgar scores, and study drug side effects were recorded. Heart rate, mean arterial pressure, oxygen saturation by pulse oximetry, eardrum temperature, chills, and degree of sedation were recorded before intrathecal injection and every 5 minutes thereafter. Patients were randomized into three groups: saline (Group C, n=30), intravenous (IV) ketamine 0.25 mg/kg (Group K-0.25, n=30) or intravenous ketamine 0.5 mg/kg (group K-0.5, n=30). Grade 3 or 4 tremor was treated with 25 mg intravenous meperidine and prophylaxis was considered ineffective.

Main Results: The number of patients with chills was significantly lower in the group 0.25 and in group K-0.5, compared to group C (P=0.001, P=0.001). Group C's eardrum temperatures were lower than both ketamine groups during the study. The mean sedation scores in the K-0.5 group were significantly higher than in the K-0.25 group or the C group at 10, 20, 30, and 40 minutes after spinal anesthesia.

Conclusion: Prophylactic IV ketamine 0.25 mg/kg was as effective as IV ketamine 0.5 mg/kg of prevents tremors in patients undergoing caesarean section under spinal anesthesia.

1. Introduction

chills are defined as noticeable seizures or tremors of the face, jaw, head, trunk or limbs lasting longer than 15 seconds [1]. Chills have been reported Loss of thermoregulatory vasoconstriction under the block causes greater loss of body heat surface exceeds metabolic heat production. East modified thermoregulation characterized by a temperature drop of 0.5°Cvasoconstriction and slightly increased sweating Threshold. The shaking is the scariest part birth experiences for patients [9].Ketamine can reduce redistribution from the center to the periphery warmth by direct central sympathetic stimulation inhibition of postganglionic norepinephrine uptake sympathetic nerve endings [10].Intravenous (IV) ketamine.0.5 mg/kg was effective in treatment and prophylaxis Chills after regional anesthesia, but many patients hallucinations [11-13].The purpose of this study was to compare efficacy and Safety of Ketamine 0.25 mg/kg Ketamine with Ketamine 0.5mg/kg as a prophylactic measure to prevent tremors patients who underwent caesarean section under spinal anesthesia.

2. Materials and Methods

120 healthy ASA pregnant women in their first and second year of life young people between the ages of 18 and 45 presenting for a planned caesarean section deliveries under spinal anesthesia were included randomized placebo-controlled trials. Patients with placenta previa, preeclampsia, Raynaud's syndrome, hypothyroidism or hyperthyroidism, cardiopulmonary disease, Mental disorders, history of allergy to drugs used in this study, initial body temperature N 38.0°C or 36°C,known history of alcoholism or drug addiction and those who required or received a blood transfusion during surgery drugs that could alter thermoregulation were excluded of the study. the temperature theater was maintained at 25^{0CC} the intravenous fluids were warmed to 37°C in a heated chamber and served in line without heating. Patient do not received premedication. Characteristics of patients and others anesthesia and surgery data, including age, ASA body condition status, body mass index (BMI), pregnancy, childbirth, indications for caesarean section, block height, amount of fluid administered intraoperative, time between spinal anesthesia and incision, time from spinal anesthesia to wound care, total estimated Blood loss was(EBL) and Apgar scores at 1 and 5 minutes checked. heart rate (HR), mean arterial pressure (MAP) oxygen saturation pulse oximetry (SpO2) were registered before the intrathecal injection and every 5 minutes thereafter in the perioperative period. Before the intrathecal injection and at 10-minute intervals in the perioperative period, eardrum temperature measured using canal thermometer and assessment of tremor were continued two hours after surgery. All patients were covered with a single blanket on chest, thighs and calves during surgery, then a cotton blanket over them whole body after surgery. All patients were active heated with convection heating. under spinal anesthesia each patient received 10 ml/kg/hours Ringer's solution with lactate. Infusion rates were then reduced to 6 ml/kg/h. Spinal anesthesia was placed at L3-L4 or L4-L5 intervals in patients in a sitting position. 3ml volumes of hyperbaric bupivacaine (Marcaine) 0.5%; 25- Quincke Needle .The patients were randomly divided into three groups consecutively numbered collection envelopes for physiological solutions (group C, n=30), ketamine 0.25 mg/kg (group K-0.25, n=30), or ketamine 0.5 mg/kg (group K-0.5, n=30). After intrathecal administration injection, medication diluted to a volume of 3mL in coded syringes was administered as an intravenous bolus by the anesthetist who were blinded to study group assignment. Supplemental oxygen (5 l/min) was delivered through a face mask during the operation. Sensory Block was evaluated by pin prick and presence of shivering were

assessed by a blind observer. There were shivering Rated on a scale similar to that approved by Tsai and Chu [14]: 0 = no tremor, 1 = piloerection or peripheral vasoconstriction but no visible tremors, 2 = muscles activities in a single muscle group, 3 = activity in the muscle group more than one muscle group, 4 = with tremors full body. The intensity of the chills was recorded at 5.minutes of rest during surgery and recovery Room. If grade 3 or 4 chills in the anesthetized patient have been reported IV meperidine (25 mg) was administered for anesthesia. side effects such as hypotension, bradycardia and nausea Vomiting, nystagmus and hallucinations were reported. if patient's heart rate fell below 50 beats per minute (bpm) Atropine IV (0.5 mg) was administered. There was hypotension defined as a MAP drop greater than 20%base and treated with crystalloid infusion and needed, IV ephedrine 5 mg. The amount of ephedrine were reported in each group. Whether the patients have developed nausea and vomiting, metoclopramide IV 10 mg was managed. Hallucination has been defined as a false sense experiences in which a patient has vision, hearing, smelled, tasted, or smelled something that wasn't there. After administration of the study drugs, the degree of sedation was determined was scored on a 5-point scale at 10-minute intervals perioperative phase [15]: 1 = fully awake and oriented, 2 =sleepy, 3 = eyes closed and excited to give orders, 4 = eyes closed but awakening with mild physical stimulation and 5='s eyes are closed but do not respond to light physical stimulation.2.1.

Statistical analysis

Statistical analysis was performed using the SPSS statistical tool Package(v26 SPSS, Continuous variables including hemodynamic data e.g temperature measurements over time in the groups were analyzed using repeated measures analysis of variance(ANOVA) followed by Bonferroni post hoc test. statistical comparisons between groups were performed using one-way ANOVA followed by Tukey's post hoc processes. Results for chills and sedation were compared using the Kruskal-Wallis test and the Mann-Whitney U test was used by Bonferroni to compare the two groups Correction if necessary. The chi-square test

Table 1. Patient characteristics, anesthetic and surgical details

	Group C (n=30) Group	K-0.25 (n=30)	Group K-0.5 (n=30)
Age (yrs)	27.3 (18-43)	26.8 (20-45)	28.2 (18-43)
ASA physical status (1/2)	25/5	27/3	25/5
Body mass index (kg/m^2)	27.8 ± 6.8	26.3 ± 6.1	26.9 ± 5.9
Gestation (wks)	38.3 ± 0.7	38.5 ± 0.6	38.6 ± 1.0
Parity 0 1 ≥2	8 15 7	5 17 8	6 15 9
Indication for Cesarean section previous Cesarean section maternal request other	20 (66%) 7 (23%) 3 (11%)	17 (63%) 9 (30%) 4 (7%)	22 (71%) 7 (23%) 1 (6%)
Sensory block cold touch	T3 (T2-T4) T4 (T3-T5)	T3 (T2-T4) T4 (T3-T4)	T3 (T2-T4) T4 (T4-T5)

Time from spinal anesthesia to incision (min)	14 ± 2.3	13 ± 3.4	15 ± 3.5
Time from spinal anesthesia to wound dressing (min)	65 ± 7	71 ± 5	68 ± 6
Apgar scores at 1st min	8 (6-9)	8 (7-9)	8 (7-9)
Estimated blood loss (L)	0.7 (0.5-0.7)	0.6 (0.5-0.8)	0.7 (0.5-0.7)
Apgar scores at 5th min	9 (8-9)	9 (8-9)	9 (8-9)
Gestation (wks)	38.3 ± 0.7	38.5 ± 0.6	38.6 ± 1.0

Data are means ± SD, medians (ranges), or numbers (proportions). Group C received saline (control group), Group K-0.25 received intravenous (IV) ketamine 0.25 mg/kg, and Group K-0.5 received IV 0.5 mg/kg.

was used for the analysis difference

between physical state ASA, number patients with chills, nausea and vomiting hallucinations. If less than, Fisher's exact test was used patients were expected. The results are presented as medians(ranges) and means (± SD) and accurate counts expressed as a percentage. The P value was 0.05were considered statistically significant.

3. Results

One hundred twenty-three patients reported study. Two patients were excluded for medical diseases and one patient due to hyperthermia. Patient characteristics and other anesthesia and operation data,, including age, ASA fitness, body mass index, pregnancy, caesarean section indication, block height, quantity intraoperatively administered fluid, time between spinal anesthesia and incisions, time between spinal anesthesia and dressing, estimated blood loss and Apgar points at 1 and 5 minutes were similar among the groups [Tab. 1]. While studying HR SpO2 values were similar in all groups. However, There were differences in MAP within groups from baseline (P value less than 0.001). IN group C had the lowest MAP scores three groups [Fig. 1].The number of patients with chills varied greatly between groups 15 minutes after spinal anesthesia (P value less than 0.001)

[Table 2]. When the post hoc comparisons were made, it was the number of patients with chills was observed much less in the K-0.25 group and in the K-0.5 group than in Group C (P=0.001 and P=0.001, respectively).There wasn't difference between the K-0.25 group and the K-0.5 group (P =0.313). In group C, 10 patients suffered from chills a grade 3 patients and two grade 4 patients. After treatment IV meperidine 25 mg ,chills stopped in all patients. NO patients in the K-0.25 group or K-0.5 group required treatment for the chills. Chills requiring treatment (≥ Grade 3)was not observed in any of the patients during this time postoperative period. There were statistically significant differences within Comparison of sets of eardrum temperature values with base values (P value 0.001). Even while tympanic temperature values were in the K-0.25 group and in the K-0.5 group At any point during the test, the tympanic membrane temperature readings are similar Group C was always lowest

[Fig. 2].mean sedation scores in the K-0.5 group were significant more than Group K-0.25 and Group C at 10, 20, 30,and 40 minutes after spinal anesthesia

[Tab. 3].Average results Group K-0.25 and Group C were similar during the study periods. Hypotensive episode data, number of doses administered Ephedrine and atropine and their side effects are shown in

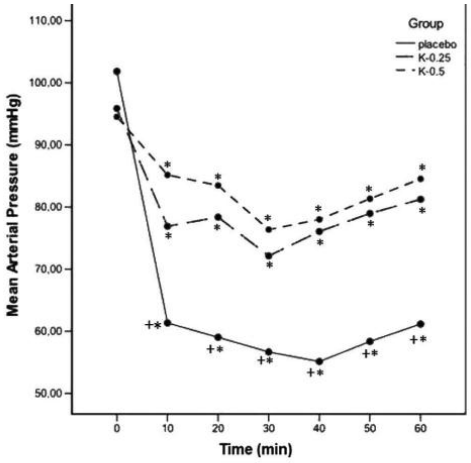

Fig. 1 Change in mean arterial pressure (MAP) with time. Data are means (SD). *Statistically significant difference within groups when compared with baseline values; +statistically significant difference between the ketamine groups and the control group. MAP decreases were statistically significant in all groups when compared with baseline levels ($P < 0.001$). $P < 0.001$, Group C vs ketamine groups; $P = 0.167$, Group K-0.25 vs Group K-0.5.

[Table 4] Incidence of hypertension, bradycardia ,Vomiting and doses of atropine and metoclopramide administered were similar in all groups. All hypotensive episodes were treated with crystalloid infusion and possibly needed, IV ephedrine 5 mg. frequency of nausea, Hypotension, tachycardia, and amount of ephedrine administered were higher in group C than in group K-0.25 or group K-0.5(P = 0.020, Pb 0.001, P=0.020, P=0.001; appropriate)[Table 4].

Side effects of ketamine such as nystagmus and hallucinations were observed more frequently in the K-0.5 group compared to the K-0 group.25 (p=0.001 and p=0.010, respectively).Amnesia was and was not reported in 9 (30%) patients in the K-0.5 group , Group K-0.25 patients (p=0.001) [Table 4].

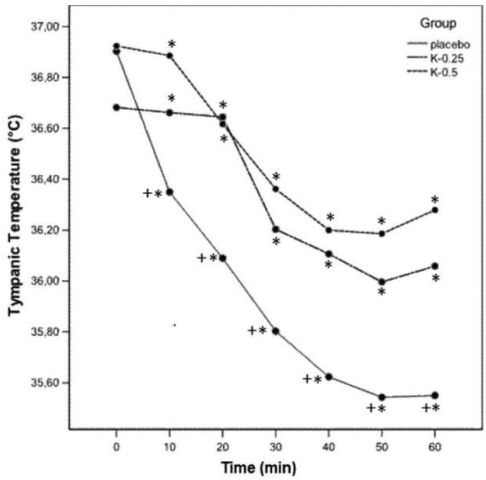

Fig. 2 Changes in core temperature with time. Data are means (SD). *Statistically significant difference within groups when compared with baseline values; +statistically significant difference between the ketamine groups and the control group. $P = 0.026$, Group C vs Group K-0.25; $P = 0.001$, Group C vs Group K-0.5.

4 -Discussion

Spinal anesthesia significantly impairs thermo regulation by inhibiting vasoconstriction, which plays a role in temperature regulation [5]. Numbers of factors such as age, degree of sensory blockade, surgical temperature, The amount of blood loss and the duration of the operation are risks Factors of hypothermia under regional anesthesia [3]. Among them, theater temperature maintained at 25^{o}C, all liquids present were rewarmed to 37°C and all patients were forced to rewarm air heating system during treatment. Other risk factors such as depending on age, degree of sensory blockage, blood loss and The duration of the operation was similar in both groups. incidence of intraoperative chills during cesarean section is said to have reached 60%.Fifteen minute after anesthesia Chills were observed in 40% of Group C patients in this study.

Relatively low frequency of chills in the control group of our study is attributable to accompanying prevention Measures to prevent the development of hypothermia, such as Warming of all patients by the circulating air warming system by warming all intravenous fluids to 37°C.core temperature drops were statistical significant in all groups from baseline(P valueless than 0.001). Also the temperature readings of the eardrum The C groups were always lower after spinal anesthesia than with They belonged to the group of ketamine or amphetamines [Fig. 2].

But The mean temperatures of the deep K-0.5 group were higher compared to the K-0.25 group, statistically this was not the case, significant difference between the two groups. Sagir et al in his study show the control group were significantly more than in the groups received ketamine [11]. The same applies to the average core temperature values in the control group were lower than in the ketamine group in the study described by Honarmand and Safavi [12].This is the relative behavior of core temperature in ketamine groups can be assigned to sympathetic stimulation and vasoconstrictor effect of the drug. more or less cases of hypotensive episodes and fewer

Table 2. Number of patients with different grades of shivering in the three groups

Grade 0/1/2/3/4			
Group C (n=30)	Group K-0.25 (n=30)	Group K- 0.5 (n=30)	
T0	30/0/0/0/0	30/0/0/0/0	30/0/0/0/0
T5	22/4/4/0/0	30/0/0/0/0	30/0/0/0/0
T10	19/3/8/0/0	29/1/0/0/0	29/1/0/0/0
T15	18/0/0/10/2	29/1/0/0/0	30/0/0/0/0

T0=baseline, T5/10/15=5, 10, 15 minutes. Group C received saline (control group), Group K-0.25 received intravenous (IV) ketamine 0.25 mg/kg, and Group K-0.5 received IV 0.5 mg/kg

Ephedrine is administered to the K-0.25 group and the K-0.5 group explained by the same mechanism [Table 4].The number of patients with chills was significantly lower in

Table 3. Sedation scores of the patients in three groups

Grade 0/1/2/3/4			
Group C (n=30)	Group K-0.25 (n=30)	Group K-0.5 (n=30)	
SS10	1 (1-1)	1 (1-3)	4 (1-5)
SS20	1 (1-1)	1 (1-3)	3 (1-4)
SS30	1 (1-2)	1 (1-2)	2 (1-4)
SS40	1 (1-1)	1 (1-2)	2 (1-3)

SS=Sedation score; SS10/20/30/40=10, 20, 30, and 40 minutes after spinal anesthesia. Group C received saline (control group), Group K-0.25 received intravenous (IV) ketamine 0.25 mg/kg, and Group K-0.5 received IV 0.5 mg/kg

Table 4. Adverse effects and amount of administered drugs for treatment in the three groups

	Group C (n=30)	Group K-0.25 (n=30)	Group K-0.5 (n=30)
Nausea	13 (43.3)	6 (20.0)	4 (13.3)
Vomiting	6 (20.0)	4 (13.3)	1 (3.3)
Hypotension	15 (50.0)	5 (16.7)	2 (6.7)
Hypertension	0 (0)	0 (0)	1 (3.3)
Bradycardia	2 (6.7)	1 (3.3)	0 (0)
Tachycardia	13 (43.3)	6 (20.0)	4 (13.3)
Nystagmus	0 (0)	3 (10.0))	16 (53.3)
Hallucination	0 (0)	0 (0)	6 (20.0)
Amnesia 0 (0) 0 (0) 9 (30.0)			
Ephedrine (mg)	13 (43.3)	2 (6.7)	4 (13.3)
Atropine (mg)	2 (6.7)	1 (3.3)	0 (0)
Metoclopramide (mg)	8 (26.7)	3 (10.0)	2 (6.7)

Data are frequencies (percentages). Group C received saline (control group), Group K-0.25 received intravenous (IV) ketamine 0.25 mg/kg, and Group K-0.5 received IV 0.5 mg/kg.

the K-0.25 pool and K-0.5 compared to group C (P=0.005,P = 0.002). Ten patients suffered from chills in stage 3 and two patients in stage 4 in group C. Patients treatment with i. v. Meperidine 25 mg, chills completely stopped . No patients in Group K-0.25 or Group K-0.5 required treatment for chills [Table 2].Ketamine causes sympathetic stimulation and vasoconstriction in patients at risk of hypothermia. ketamine that is a competitive N-methyl-D-aspartate receptor antagonist Acid(NMDA) plays a role in thermoregulation at multiple levels .NMDA receptors modulate noradrenergic receptors, e .g serotonergic neurons at the locus coeruleus and there with NMDA receptors in the dorsal horn of the spinal cord[16]. Ketamine has other pharmacological properties such as by blocking uptake in the descending inhibitory monoamine gene pain pathways that interact with muscarinic receptors local anesthetic and kappa opioid agonist. Ketamine probably controls tremors by non-shivering thermogenesis, either by action on the hypothalamus, or byβ-adrenergic effects of norepinephrine [13]. Precise The mechanism of action of Ketamine is not clear [11-13,16]. Mean sedation score in the K-0 group was more than the K-0.25 group at 10, 20, 30, and 40 minutes study. There were no statistically significant differences between Group K-0.25 and Group C for sedation points at each time point [Table 3]. In this study (30%) of patients in the K-0 group. did not remember the events of childbirth due to strong sedative and amnesiac effects ketamine. However, none of the patients in the groupK-0.25 had sedation scores greater than 3 or reported Amnesia [Tab. 3, 4].nystagmus and hallucinations, known side effects Ketamine was more common in the K-0.5 group than in the K0.25 group [Table 4]. While Sharma and Thakur [13] reported about it, two of the 20 patients in their study had hallucinations observed due to IV administration of 0.5 mg/kg ketamine hallucinations in 6 of 30 patients in the K-0.5 group and none patients in the K-0.25 group. Ketamine 0.25 mg/kg intravenously

was as effective as IV Ketamine 0.5 mg/kg for the prevention of tremors in patients with caesarean section under spinal anesthesia showed no serious side effects.

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