ORIGINAL ARTICLE

Prophylactic Ketamine Reduces Incidence of Postanaesthetic Shivering

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Abstract

Background: *General anesthesia influences the thermoregulatory process. The aim of this study was to compare the efficacy of low-dose prophylactic ketamine with that of placebo in preventing postoperative shivering.*

Methods: *A prospective randomized double-blind study involved 76 ASA I and II patients undergoing general anesthesia that was expected to last no more than 2 hours. Patients were randomly allocated to receive normal saline (Group P, n=33) or ketamine 0.5 mg kg^{1} (Group K, n=33) intravenously 20 min before completion of surgery. The anesthesia was induced with propofol 2.5-3.0 mgkg^{-1} and fentanyl (2 -3 μgkg^{-1}), atracurium 0.5 mgkg^{-1}) was given to facilitate orotracheal intubation. It was maintained with propofol (510 mgkg^{-1}hr^{-1}), fentanyl up to (5 μg · kg^{1} · h$^{1)}$ and a mixture of nitrous oxide/oxygen (2:1). Ambient temperature was maintained at 20°22°C with constant humidity. Postoperative shivering in the recovery room was evaluated according to 5 point scale of Wrench.*

Results: *The two groups did not differ significantly regarding patient characteristics. The number of patients shivering on arrival in the recovery room, and at 10 and 20 min after operation was significantly less in Groups K than in Group P. In group P 36% have had shivering in T0 whereas in group K 6%, in T10 45% in group P whereas 18% in group K. In T 20 24% in group P have had shivering compared with 6% in group K, whereas in T30 9% in group P compared with 0% in group K. The incidence of free Postanaesthetic shivering (no shivering) on arrival in the recovery room T0 was: 63.6% in group P compared with 90.9 % in group K. The postoperative hemodynamic parameters were similar in the two groups. Active warming was not required in group K but was needed in 8 cases in group P.*

None of patients had episodes of O_2 desaturation or respiratory depression during the study period. No hallucinations, delirium, nausea, vomiting, hypertension, tachycardia, and feeling like walking in the space or nystagmus were seen in any of the patients.

Conclusion: *Prophylactic low-dose ketamine was found to be effective in preventing postoperative shivering.*

Date Accepted for Publication: 18th October 2009
NigerJMed 2010:

Introduction

Post-anesthetic shivering is a rhythmic oscillating movement, predominantly involving upper limbs, neck and jaw; it occurs in 565% of patients after general anesthesia and 33% of patients undergoing epidural regional anesthesia. Perioperative hypothermia is an unintentional drop in the core body temperature to less than 36°C during or immediately following a surgical operation. This may be normal thermoregulatory shivering due to core hypothermia or may result from release of cytokines by surgical procedure. The core temperature usually decreases by 0.5-1.5 °C in the first hour after induction of anesthesia. All general anesthetics markedly impair normal autonomic thermoregulatory control. Contributing factors vary and include extremes of age, low ambient room temperature, length and type of surgical procedure, use of cold irrigants and the type of anesthesia [2].

Perioperative hypothermia may cause complications, especially in patients with coronary artery disease, because of associated increases in oxygen consumption (by 100600%), cardiac output, carbon dioxide production, and circulating catecholamines, and a significant decrease in mixed venous oxygen saturation. In patients with compromised cardiac function, there is increased risk of cardiac arrhythmias, angina pectoris and myocardial infarction in the subsequent 24 hours after surgery . Moreover, shivering may exacerbate postoperative pain, an increase in intracranial and intraocular pressure, hypoxemia, raised carbon dioxide production [1] increased metabolic rate, and lactic acidosis have been described in shivering patients.[4 5 6] This could be associated with post operative instability and prolonged recovery .

Our objective was to investigate the efficacy of prophylactic ketamine in preventing postoperative shivering.

Materials and Methods

This prospective, randomized, double-blind study was performed after obtaining approval from our hospital ethical committee and informed consent from 76 patients, aged 18-65 ,ASA class I or II who had undergone elective abdominal, orthopedic, and

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maxillofacial surgery under general anesthesia that was expected to last no more than 2 hours. Patients who received blood products, metoclopromide, Body Mass Index >30 kg/m^2, those with a history of convulsions, multiple allergies, hypertension, coronary artery disease, other cardiorespiratory or neuromuscular pathology or if use of vasoconstrictors or vasodilators was planned, were excluded from the study.

The patients were randomly allocated to receive placebo (saline 0.9%) IV (control group, *n* = 33) or ketamine 0.5 mg/kg IV (ketamine group, *n* = 33). The treatment drugs were diluted to a volume of 2 mL and presented as coded syringes by an anesthesiologist who was not involved in the management of the patients or in grading of the patients' shivering. On arrival in the OR, intravenous access was obtained with an 18 gauge IV canula and standard monitoring electrocardiogram (3 lead), noninvasive blood pressure, pulse oximeter were connected and the baseline vital parameters were noted. All patients received midazolam 0.03mg/kg i/v as a premedication 10 minutes before induction and were preoxygenated with 100% O2 for 5 minutes. In the both groups anesthesia was induced with propofol 2.5-3.0 $mgkg^{-1}$ and fentanyl (2 -3 μgkg^{-1}), atracurium 0.5 $mgkg^{-1}$) was given to facilitate orotracheal intubation. It was maintained with propofol (510 $mgkg^{-1}hr^{-1}$), intraoperative analgesia was provided by fentanyl up to 5 $\mu g \cdot kg^{1} \cdot h^{1}$. Controlled ventilation was performed with a mixture of nitrous oxide/oxygen (2:1), to maintain end tidal CO2 at 30-35 mmHg. Increments of atracurium 0.2 mg/kg were given if needed.

Patients had standard cotton surgical drapes and were not actively heated. Ambient temperature was maintained at 20°22°C with constant humidity. Depending on the group to which the patient belonged, approximately 20 minutes before the end of operation, patients received (saline 0.9%) IV or ketamine 0.5 mg/kg IV. At the end of the procedure residual neuromuscular block was reversed with neostigmine up to 0.04mg kg-1 and atropine sulphate 0.02 mg kg-1 and extubated in awake state. After that the patients were transported to the postanaesthetic care unit (PACU).

After the patient arrived in the PACU, an investigator who was blinded to the intraoperative management recorded the incidence and severity of shivering. In the recovery room, all patients were covered with a standard cotton blanket, none of them was warmed actively and all received 4 L/min oxygen by facemask. Postoperative shivering in the recovery room was evaluated according to 5 **point scale of Wrench Shivering** was defined as readily detectable fasciculations or tremors of the face, trunk, or limbs of a minimum of 15-s duration. Side effects that may have been related to the study drugs (i.e., nausea, vomiting, hypotension, hypertension, tachycardia, nystagmus, feeling like walking in the space, and hallucinations) and a sedation score (using a four-point scale) were also recorded. The shivering was treated with ketamine10- 20 mg i.v. if the shivering grade was 2

Patients rated their satisfaction with the anesthesia by using a five-point scale (1 = very satisfied; 2 = somewhat satisfied; 3 = neither satisfied nor dissatisfied; 4 = somewhat dissatisfied; 5 = very dissatisfied) approximately 24 h after anesthesia.

Table I. The 5 point scale of Wrench

Score	Definition
0	No shivering
1	One or more of: piloerection, peripheral vasoconstriction, peripheral cyanosis without other cause, but without visible muscular activity
2	Visible muscular activity confined to one muscular group
3	Visible muscular activity in more than one muscle group
4	Gross muscular activity involving entire body

Results

There were no significant differences between the groups with respect to demographic data, ASA score

The incidence of severity of PAS at 0 min, 10, 20, 30 minutes was significantly less in group K than in group P.

In group P 36% have had shivering in T0 whereas in group K 6%, in T10 45% in group P whereas 18% in group K. In T 20 24% in group P have had shivering compared with 6% in group K, whereas in T30 9% in group P compared with 0% in group K.

The incidence of free postanaesthetic shivering (no shivering) on arrival in the recovery room T0 was: 63.6% in group P compared with 90.9 % in group K. In T30 the incidence of free postanaesthetic shivering was 93.9% in group P compared with 100% in group K.

The postoperative hemodynamic parameters were similar in the two groups. Active warming was not required in group K but was needed in 8 cases in group P.

None of patients had episodes of O_2 desaturation or respiratory depression during the study period. No hallucinations, delirium, nausea, vomiting hypertension, tachycardia, and feeling like walking in the space or nystagmus were seen in any of patients.

None of patients suffered from the 4th degree of the Wrench scale in either of the groups.

Table II Demographic data

Data are presented as mean ± SD.

Demographic data	Gr. P(placebo)	Gr. K (ketamine)
N	33	33
Age (Mean ± SD)	29.2 ± 13.2	32.0 ± 15.3
Weigh (Mean ± SD)	71.2 ± 12.1	68.6 ± 11.4
Height (Mean ± SD)	169.0 ± 7.5	171.2 ± 7.34
Sex M\F	16/17	19/14
ASA score I/II	21/12	23/10

Table III Number of patients with different grades of shivering in the two treatment groups.

	Group P (placebo), n 33					Group K (ketamine), n 33				
Score	0	1	2	3	4	0	1	2	3	4
T 0	21(63.6%)	4(12%)	2(6%)	6(18%)	0(0%)	30(90.9%)	1(3%)	0(0%)	2(6%)	0(0%)
T 10	18(54.5%)	4(12%)	3(9%)	8(24%)	0(0%)	28(84.8%)	2(6%)	1(3%)	3(9%)	0(0%)
T 20	25(75.7%)	3(9%)	3(9%)	2(6%)	0(0%)	31(93.9%)	1(3%)	0(0%)	1(3%)	0(0%)
T 30	31(93.9%)	1(3%)	0(0%)	1(3%)	0(0%)	33(100%)	0(0%)	0(0%)	0(0%)	0(0%)

T0, arrival in the recovery room; T10, 10 min after arrival; T20, 20 min after arrival; T30, 30 min after arrival.

Discussion

Postoperative shivering is very unpleasant and physiologically stressful. Hypoxemia, lactic acidosis and hypercarbia may be associated with severe shivering and may complicate recovery from anesthesia. We found that administration of ketamine 20 minutes before the end of surgery reduced the incidence and severity of shivering.

Various drugs have been investigated for prevention or treatment of postoperative shivering, including pethidine, sufentanil, alfentanil, tramadol, physostigmine, urapidil, nefopam, doxapram and nalbuphine[4, 5, 6, 11, 12] but the ideal treatment has not yet been found. Ketamine, a competitive NMDA receptor antagonist, also inhibits postoperative shivering. It is likely that NMDA receptor antagonists modulate thermoregulation at a number of levels. In addition to being a competitive NMDA receptor antagonist, ketamine has several other pharmacological properties; these include being an opioid agonist, blocking amine uptake in the descending inhibitory monoaminergic pain pathways, having a local anesthetic action and interacting with muscarinic receptors. Therefore it probably controls shivering by non-shivering thermogenesis either by action on the hypothalamus or by the ß-adrenergic effect of norepinephrine. We chose a dose of 0.5 mg kg[1] because the higher dose of ketamine was also associated with adverse side effects in previous studies and because some authors also report that ketamine 0.5 mg/kg IV was effective for the treatment of postoperative shivering.[15]

The incidence of free postanesthetic shivering (no shivering) on arrival in the recovery room T0 was: 63.6% in group P compared with 90.9 % in group K, which is in accordance with other studies.[4]Postoperative shivering is a common phenomenon, and in our placebo group the incidence was 45% -10 minutes after arrival in recovery room whereas in ketamine group 18%, a proportion that is not similar to that reported in other studies.[4]

This has been attributed to the following factors: uninhibited spinal reflexes, pain, decreased sympathetic activity, adrenal suppression, release of pyrogenic mediators during surgery, administration of volatile anesthetics, opiate withdrawal, blood loss, duration of surgery and thermoregulatory shivering in response to intraoperative hypothermia.

The authors also reported that two patients had developed hallucinations and four patients had developed delirium in one study.[15] We did not observe hallucinations or delirium in any of our patients when ketamine was given 20 min before completion of surgery under general anesthesia, however, these are well-known side effects of ketamine.

None of patients had episodes of O_2 desaturation or respiratory depression during the study. No symptoms of nausea, vomiting, hypertension, tachycardia, feeling like walking in the space or nystagmus was seen in any of patients.

Conclusion: The prophylactic use of 0.5 mg/kg i.v. ketamine 20 min before completion of surgery was effective in preventing shivering developing after general anesthesia, without significant adverse side effects.

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