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# The Effect of Low-Dose Ketamine on Prevention of Hypotension Due to Positioning After Induction of General Anesthesia in Lumbar Disc Surgery

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## Abstract

**Objectives:** This study aimed at investigating the effect of low-dose ketamine on prevention of hypotension due to positioning after induction of general anesthesia in lumbar disc surgery.

**Materials and Methods:** This double-blind clinical trial was performed during a 3-month period in 2016. A random sample of 84 patients with ASA (American Society of Anesthesiologists), class I, were enrolled in the study and the impact of ketamine on prevention of hypotension due to repositioning was investigated. After induction of anesthesia and intubation, ketamine 0.5 mg/kg of body weight as well as normal saline solution, with equal volumes, were injected to the intervention and control groups, respectively. Patients were repositioned though a similar method to prone position after peak of ketamine (after 1.5 minutes), and then, systolic, diastolic, and mean of the blood pressure were measured as a baseline, once before and 1 minute after the intubation, before repositioning, immediately after repositioning the patient from supine to prone position, and then every 2 minutes until 10 minutes after repositioning.

**Results:** There was significant differences in means (SDs) of systolic pressure and blood pressure in the first, second, and fourth minutes after repositioning, as systolic pressure and mean of the blood pressure in ketamine group was higher than those of control group. The changes of blood pressure in ketamine group was the least amount after repositioning.

**Conclusions:** Ketamine can increase blood pressure, especially systolic pressure of patients, on other hand changes of blood pressure in ketamine group after repositioning was least amount.

**Keywords:** Ketamine, Hemodynamic changes, Lumbar disc surgery, Repositioning

## Introduction

Spine surgical procedures are one of the usually performed procedures worldwide (1); patients are commonly placed in a prone position, after induction of general anesthesia, prone position, and anesthesia caused hypotension (1,2).

The prone position has been used and developed for spine surgical access. Ideal patient positioning in these procedures include balancing surgical comfort against the risks related to the patient position. Therefore, patient positioning during surgery should be considered in preoperative evaluation (3).

Positioning for patients with neurosurgical problems is important and challenging; it requires adequate anesthetic depth, stability of hemodynamic, and adequate oxygenation (4,5). According to previous studies, after turned prone position, sympathetic activity increased (increased heart rate, total peripheral vascular resistance, hypotension, and plasma noradrenaline); in addition, anesthetic technique was found to affect hemodynamic variables (6). This finding could be contributed to a decrease in arterial filling because of increased intrathoracic pressure and reduced venous return and that left ventricular compliance might also decrease due to increased intra-thoracic pressure (7,8).

Currently, propofol is the most common drug used for induction of anesthesia around the world and also in our treatment centers. It was observed that it causes a decrease in blood pressure after injection and as a result, it is considered as a common side effect in this respect. In addition, reduction of blood pressure in patients who are undergoing lumbar disc surgery after induction of anesthesia and must also be repositioned, is a major concern for anesthesiologists (9).

One solution to prevent hypotension after induction of anesthesia with propofol is to add ketamine to anesthetic drugs. Atashkhoyi et al showed that in patients undergoing gynecologic laparoscopy, addition of low dose of ketamine to propofol during induction anesthesia resulted in less

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consumption of propofol, and therefore, less reduction in blood pressure (10). Several studies demonstrated that ketamine was one of the safest anesthetic drugs (11-14). It was used for many years owing to be as safe as a medicine, particularly for maintaining cardiovascular and hemodynamic stability (15). The primary site of ketamine action was on the CNS (thalamocortical pathways and the limbic system, that is central nervous system). In fact, it weakened the thalamus and stimulated the cortex and the limbic system, particularly the hippocampus, and thus caused catecholamine release and increased heart rate, blood pressure, and cardiac output (9).

Intravenous dose of ketamine is 1-2 mg/kg of body weight and its supplementary doses is 0.25 or 0.5 mg every 10 minutes (9,16,17).

Every day, notable extent of lumbar disc surgeries are performed in Shohada medical research and training center of Tabriz within the neurosurgery ward, but reduction of blood pressure after induction of anesthesia and repositioning is worrying. Reviewing the literature, researchers of the present study were not confronted with studies on clinical trials to prevent a reduction of blood pressure due to repositioning to prone as a result, this study was designed in order to focus more on the above-mentioned issue.

This study aimed to explore the effect of low-dose ketamine on prevention of hypotension due to positioning after induction of general anesthesia in lumbar disc surgery.

## Materials and Methods

This double-blind clinical trial was conducted in Shohada medical research and training center of Tabriz University of Medical Sciences from June to September 2016. It was called a double-blind trial, because the patients, the operator of injections (who did the injection), and the data recording operator were unaware about the type of injected medicine in all the steps.

### Study Samples

Patients with American Society of Anesthesiologists (ASA) class I, who were candidate for lumber disc surgery and referred to Shohada medical research and training center of Tabriz University of Medical Sciences for medical treatment. They were enrolled in the study through random sampling technique. The process of randomizing the patients in 3 groups was conducted using an online software (https://www.graphpad.com/quickcalcs/randomize1.cfm). The participants were examined more carefully in terms of inclusion and exclusion criteria. Comprehensive information on research objectives, its benefits, confidentiality of the collected data, and research procedure was provided to them. All the eligible subjects were enrolled in this study and were asked to complete an informed consent. Then, they were randomly assigned into two groups.

### Sample Size

According to a previous study (power of 80% and given 10% difference in reduction of blood pressure), 76 patients were required (10). Considering 10% dropouts of the sample, a total of 84 patients were recruited, cooperated with the researchers up to the end of the study, and consented to proceed with the study protocol. All the eligible patients were randomly assigned, on a 1:1 ratio, into intervention and control groups (n= 42 in each groups). The intervention group was injected .5 mg of ketamine per kg of body weight whereas the control group (n= 42) received equal volume of normal saline solution (equal injected volumes for both group). Researchers with no clinical involvement in the trial, enrolled the subjects and divided them into groups.

### Inclusion Criteria

- Patients with ASA class I, who were candidate for lumber disc surgery, and
- Aged 20 to 40

### Exclusion Criteria

- High class of ASA for any reason,
- History of cardiovascular drugs use,
- History of psychotic drugs use and psychotic diseases,
- Emergency surgery,
- Cardiovascular diseases, and
- BMI (body mass index) > 40

These 2 groups were distinguished according to proprietary code so that neither the participants of the study nor the assessors or recorders of variables were informed of the actual grouping. Medicines were prepared by an anesthesiologist, coded in similar syringes by a non-involved person, and given to the researcher. Method of induction of anesthesia in all groups was similar. It was carried out following the preparation in surgery room and stablishing an intravenous line, prehydration, and hemodynamic monitoring and included midazolame (0.03 mg/kg), fentanyl (2 μ/kg), propofol (1-2.5 mg/kg), and atracurium (0.5 mg/kg) in the supine position. After induction of anesthesia and intubation, ketamine (0.5 mg/kg) and normal saline solution (with equal volumes) were injected into participants of intervention and control groups. Patients were repositioned through a similar method to prone position after peak of ketamine (after 1.5 minutes).

Endotracheal intubation was done, when the fourth TOF (train-of-four) response was destroyed (after 30 seconds) by using a peripheral nerve stimulator. The variables studied include systolic, diastolic, and mean of blood pressure as a baseline, once before and one minute after the intubation, before repositioning, immediately after repositioning the patient from supine to prone position, and then every 2 minutes until 10 minutes after the repositioning; if the decrease of blood pressure was greater than 20% of the base, ephedrine 5 mg (if heart rate was less than 100) or phenylephrine 10 mg (if heart rate was more than 100) were used and repeated as necessary. Patient monitoring-anesthesia management and data recording-questionnaire completion were conducted by 2 anesthesiologists who were unaware about the type of injected medicine in all the steps.

### Statistical Analysis

Data were analyzed and examined using descriptive statistical methods, that is, mean SD), frequency (%), independent samples *t* test, the chi-square test and SPSS software, version 15. In this study, $P \leq .05$ was considered as statistically significant. Besides, all the data had a normal distribution.

## Results

All eligible patients were willing to participate in the study and no one refused to cooperate. A total of 84 patients enrolled in the study. About 39 (46.4%) patients were males and 45 (53.6%) of them were females. The mean age of intervention group was 34.5 (4.4) while being 35.6 (4.6) for the control group. In terms of gender, age, and baseline hemodynamic variables (systolic blood pressure (SBP), diastolic blood pressure (DBP), mean of blood pressure (MBP), and heart rate), there was not any significant difference ($P > 0.05$) between the groups; this showed that there was a concordance between the 2 groups in terms of the above-mentioned variables (Table 1). No vasopressor was used for any patient during the operation.

The results showed that there was no significant difference in means (SD) of systolic, diastolic and blood pressure, and also heart rate between the groups before, one minute after intubation, and immediately after repositioning ($P > 0.05$); this showed a conformity of evaluated factors of the 2 groups (Table 2).

The results revealed that there was a significant difference in the means (SD) of systolic pressure, diastolic pressure, and blood pressure between the groups, one minute after repositioning ($P = 0.001$, $P = 0.001$, $P = 0.002$, respectively), 2 minutes after repositioning ($P = 0.007$, $P = 0.033$, $P = 0.006$, respectively), and 4 minutes after repositioning ($P = 0.009$, $P = 0.014$, respectively), as these factors were higher in ketamine group as compared to control group, but there was not any significant difference of heart rate ($P > 0.05$) between the groups; this also showed a concordance of the 2 groups (Figure 1).

However, the results showed that there was not any significant difference in the means (SD) of systolic, diastolic, blood pressure, and heart rate in the 6th, 8th, and 10th minutes after repositioning ($P > 0.05$); this showed that there was a conformity between the 2 groups (Table 3).

**Table 1.** The Gender, Age, and Baseline Hemodynamic Differences Between the 2 Groups Using Chi-square and Independent Samples *T* Test (n = 84)

| Variables | Ketamine | Control | *P* Value |
|---|---|---|---|
| Gender, No. (%) | | | 0.191 |
| Male | 22 (52.4) | 17 (40.5) | |
| Female | 20 (47.6) | 25 (59.9) | |
| Age, mean (SD) | 34.5 (4.4) | 35.6 (4.6) | 0.301 |
| Baseline hemodynamic variables, mean (SD) | | | |
| SBP, No. (%) | 128.7 (13.3) | 128.7 (11.5) | 0.998 |
| DBP, No. (%) | 82.8 (9.0) | 83.8 (12.0) | 0.668 |
| MBP, No. (%) | 98.2 (8.8) | 96.7 (12.3) | 0.552 |
| Heart Rate, No. (%) | 83.2 (15.2) | 87.1 (13.8) | 0.217 |

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean of blood pressure.
Note: *P* value <0.05 is significant.

**Table 2.** Means (SDs) of Systolic Pressure, Diastolic Pressure, Blood Pressure, and Heart Rate of Before, 1 Minute After Intubation, and Immediately After Repositioning, by Independent Samples *T* Test (n=84)

| Variables | Ketamine Mean (SD) | Control Mean (SD) | *P* Value |
|---|---|---|---|
| Before intubation | | | |
| SBP | 108.5 (17.8) | 108.7 (15.0) | 0.947 |
| DBP | 68.1 (15.0) | 69.3 (12.4) | 0.676 |
| MBP | 82.2 (15.5) | 81.7 (13.2) | 0.880 |
| Heart Rate | 80.6 (13.8) | 83.1 (14.3) | 0.355 |
| One minute after intubation | | | |
| SBP | 131.9 (11.6) | 123.9 (22.9) | 0.048 |
| DBP | 87.5 (12.2) | 81.9 (15.3) | 0.067 |
| MBP | 102.4 (10.4) | 96.1 (18.5) | 0.058 |
| Heart Rate | 91.6 (17.3) | 91.5 (17.3) | 0.994 |
| Immediately after repositioning | | | |
| SBP | 122.8 (13.4) | 116.9 (20.0) | 0.119 |
| DBP | 77.8 (11.9) | 77.1 (16.5) | 0.838 |
| MBP | 93.9 (11.8) | 90.2 (17.9) | 0.273 |
| Heart Rate | 89.9 (14.6) | 90.4 (11.8) | 0.607 |

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean of blood pressure.
Note: *P* value <0.05 is significant.

## Discussion

This study investigated the effect of low-dose ketamine on prevention of hypotension owing to positioning after induction of general anesthesia in lumbar disc surgery. The results indicated that there was a significant difference in mean (SD) of systolic pressure in two groups and that systolic pressure was higher in ketamine group than control group. Meanwhile, a decrease of blood pressure after repositioning in ketamine group was found to be minimum.

However, the results showed that there was no significant difference in systolic, diastolic, mean of blood pressure and heart rate between the groups at baseline and before the intubation. This means that there was a concordance

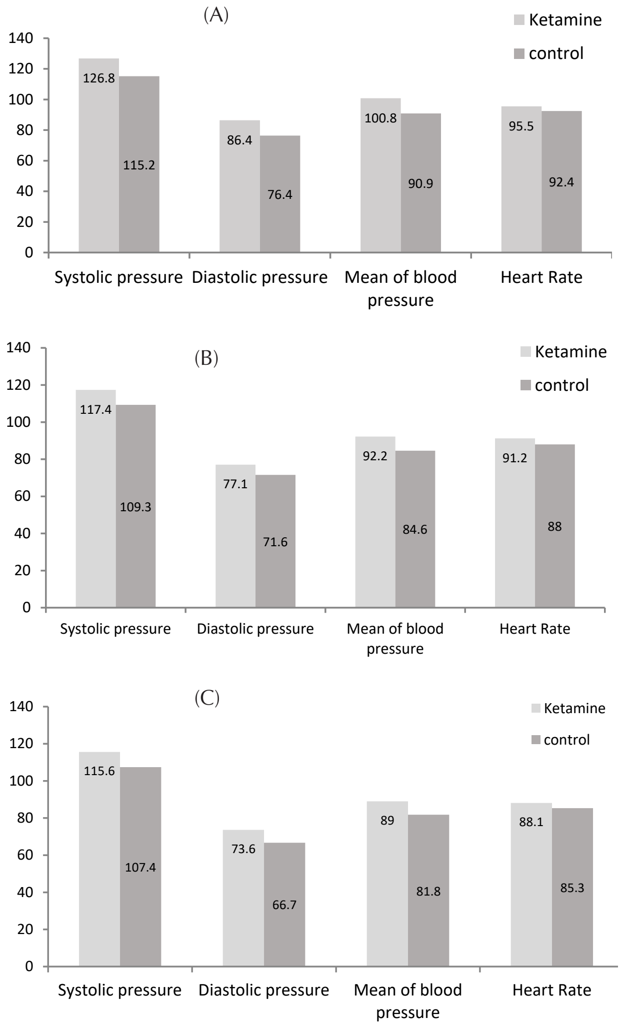


**Figure 1.** Mean (SD) of Systolic, Diastolic, Mean of Blood Pressure and Heart Rate of Groups on (A) 1, (B) 2 , and (C) 4 Minutes After Repositioning by Independent Samples *T* Test (N = 84).

between the evaluated factors of the two groups and that they were ineffective on the following outcomes.

Blood pressure increased after intubation in both groups but it was significantly higher in ketamine group; this could be due to the injection of ketamine (this was an expected effect of ketamine), which is consistent with the results of the study by Hosseinzadeh et al (18). Moreover, Garg et al (19) showed that the combination of ketamine and propofol could develop greater hemodynamic stability. This is in line with the results of the present study.

Similarly, no significant difference was found in systolic, diastolic, mean of blood pressure, and heart rate before repositioning in both groups; this could be due to the activation of blood pressure compensator systems.

Conversely, however, a significant difference was observed in systolic, diastolic, and mean of blood pressure between the groups after repositioning; the mean blood pressure increased in ketamine group while it decreased in control group before repositioning. These changes could be due to the expected effect of ketamine since cardiovascular function is affected by prone position. That is, it decreases cardiac output and consequently decreases blood pressure (20,21).

The results revealed that there was a significant difference in systolic, diastolic, and mean blood, one minute after repositioning. According to previous results and in comparison with other similar studies in this context, maintenance stability of blood pressure could be due to ketamine. In addition, this significant difference was kept in the second minute after repositioning. However, in the fourth minute after repositioning, a significant difference was observed in systolic pressure and mean blood pressure in patients of the 2 groups. Considering the initial significant increase of systolic pressure after injection of ketamine, it can be stated that this could be due to the great effect of ketamine on systolic pressure. According to the formula of mean blood pressure the significant difference of this factor could be justifiable. Although, there was not any significant difference in systolic, diastolic, and mean blood pressure in the 6th, 8th, and 10th minutes after repositioning.

However, in comparison of systolic pressure, diastolic pressure, and mean blood pressure in 6th, 8th, and 10th minutes after repositioning, these factors decreased because of hemodynamic change due to repositioning, but, the level of decrease in ketamine group was less than that of the control group, so, ketamine could increase blood pressure.

## Conclusions

Ketamine can increase blood pressure, especially systolic pressure of patients, on other hand changes of blood pressure in ketamine group after repositioning was least amount.

## Conflict of Interests

Authors have no conflict of interests.

## Ethical Issues

Before beginning the study, the research protocol was approved by Ethics Committee of Tabriz University of Medical Sciences January 14, 2016 (Ethics code: 94/3-12/24) and registered in the Iranian Registry of Clinical Trials website (identifier: IRCT2016062726328N2). In addition, participants were informed of the research procedures, objectives, and benefits. A signed consented form was obtained prior to data collection.

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