Original Article

Effect of Ketofol instead of Propofol on hemodynamic stabilization for induction of anesthesia in laparatomy

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Abstract

Background: Hemodynamic alterations are a common complication during anesthetic induction with intravenous anesthesia. Hypotension due to propofol injection may be very severe in cardiac vascular patients. Ketamine produces increasing significantly, but temporary effect on systematic blood stream, heartbeat, and cardiac output through central sympathetic stimulation. The aim of the study was to determine effect of ketofol and propofol for induction of anesthesia on hemodynamic changes during induction of anesthesia.

Materials and Methods: In the randomized clinical trial study, 96 patients who were candidate for laparotomy enrolled and divided into two random groups of propofol (48 person) and ketofol (48 person). Hemodynamic changes were recorded and examined after induction for 5 and 10 minutes after intubation.

Results: Heart rate was significantly variable in propofol group compared to ketofol group. Systolic, diastolic, and mean arterial blood pressure was not significantly changed during the time period of recording in ketofol group. However, blood pressure was significantly changed during the study in the propofol group.

Conclusion: ketofol is a proper alternative to propofol to stabilize heart rate and blood pressure in laparotomy.

Keywords: Ketofol, Hemodynamic, Anesthesia, Laparatomy

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Introduction

Hemodynamic instability is a major complication of anesthesia due to induction, intubation, surgical incision and stress, hypovolemia, anesthesia drugs and volatile anesthetics. Surgical incision and pain cause increase in blood pressure and heart rate.

This challenge is more prominent in patients with ischemic heart diseases, valvular heart diseases, and other cardiovascular diseases. Drugs used for induction of anesthesia decrease blood pressure acutely. Propofol decreases blood pressure by several mechanisms; however, ketamine increases blood pressure vice versa.

Propofol is used at a dose of 1-2.5 mg/kg for induction of anesthesia. Old age, decrease of cardiac reserve and premedication with benzodiazepines and opioids decreases the required dose for induction of anesthesia. Propofol increases the influx of Cl through Cl channels by an effect on GABA receptors.

Ketamine is an antagonist of NMDA receptors could increase systolic and diastolic blood pressure and heart rate by stimulation of sympathetic system. These effects are modified by opioids or volatile anesthetics. Induction of anesthesia is performed by 1-2 mg/kg intravenously or 4-6 mg/kg through intramuscular. Ketamine causes hypnosis and analgesia. Ketamine passes the brain blood barrier and its peak of action is 1 minute by drug redistribution from the brain into the blood stream and then other tissues. The onset of effect of ketamine is 15-30 seconds after intravenous (IV) administration and 3-4 minutes after intramuscular (IM) injection. Duration of effect is 5-10 minutes after IV and 12-25 minutes after IM injection. Propofol rapidly redistribute in blood and other tissues.

Propofol mixed with ketamine (ketofol) is a popular for short procedural sedation and analgesia (1). Ketofol is a combination of the same amount of propofol and ketamine administered for induction of anesthesia. There are a number of recent studies demonstrating the beneficial effects of combination of ketamine and propofol (2); providing cardiovascular stability (3) which could be comparable to etomidate; on the other hand, this combination does not lead to adverse effects of etomidate-associated adrenal insufficiency in critically ill or septic patients (4).

Although in recent studies ketofol has been used for sedation in the emergency department or critically ill patients in ICU (5-7), there are no reports evaluating the use of “ketofol” for induction of anesthesia in elective surgeries. The aim of the study was to determine effect of ketofol and propofol for induction of anesthesia on hemodynamic changes during induction of anesthesia.

Methods

The study was reviewed and approved by the Shahid Beheshti University of Medical Sciences Ethics Committee and been performed in accordance. Information about the study was given comprehensively both orally and in written form to all patients or their accompanying adult. They gave their informed written consent prior to their inclusion in the study.

In a randomized clinical trial, 96 patients candidate for elective laparotomy and ASA class I,II were enrolled and randomly assigned to ketofol and propofol group. Study was performed in a 12 month period from 2014 to 2015.

Exclusion criteria included patients with hypotension or uncontrolled hypertension prior to surgery, heart rate less than 50, pacemaker, bleeding diathesis, difficult intubation or more than 3 attempts for intubation, and required a transfusion prior to surgery.

Groups of study and monitoring

Patients were induced by ketofol in the ketofol group and by propofol in the propofol group. For ketofol group, Ketamine and propofol mixture (ketofol) was prepared 5 mg/mL ketamine and 5 mg/mL propofol, 1:1 mixture in a 20-mL syringe.

Patients were admitted to the operating room and were monitored for pulse oximetry, arterial line, and invasive blood pressure monitoring, electrocardiogram, capnography, bispectral index (BIS) for depth of anesthesia, and cerebral oximetry. Hemodynamic parameters (systolic arterial pressure (SAP), and heart rate (HR) were recorded by an anaesthetist who was blinded to the patient group, at times baseline 0 minutes, and after induction, then after intubation, and the 5 and 10 minutes after intubation.

Induction of anesthesia

Patients were pre-hydrated with 350 ml of normal saline. For pre-medication, Midazolam 0.02 mg/kg and fentanyl 2 µg/kg was administered. After 3 minutes pre-oxygenation, for induction of anesthesia, in Ketofol group, ketofol 1.5 mg/kg and in propofol group 1.5 mg/kg was administered. Then Atracurium 0.5 mg/kg was administered for proper muscle relaxation.

After 3 minutes, patients were intubated with appropriate sized cuffed endotracheal tube. Anesthesia was maintained using propofol 100 µg/kg/min and the mixture of N2O 50%/O2 50%. All intubations were performed by the same anesthesiologist.

Blood pressure and heart rate were recorded prior to induction, 3 minutes after induction, after intubation, and 5 and 10 minutes after induction.

Results

In this study, 96 patients candidate for elective

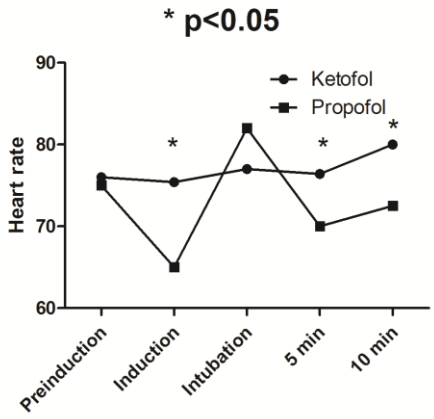

Figure 1. Heart rate in ketofol compare to propofol group.

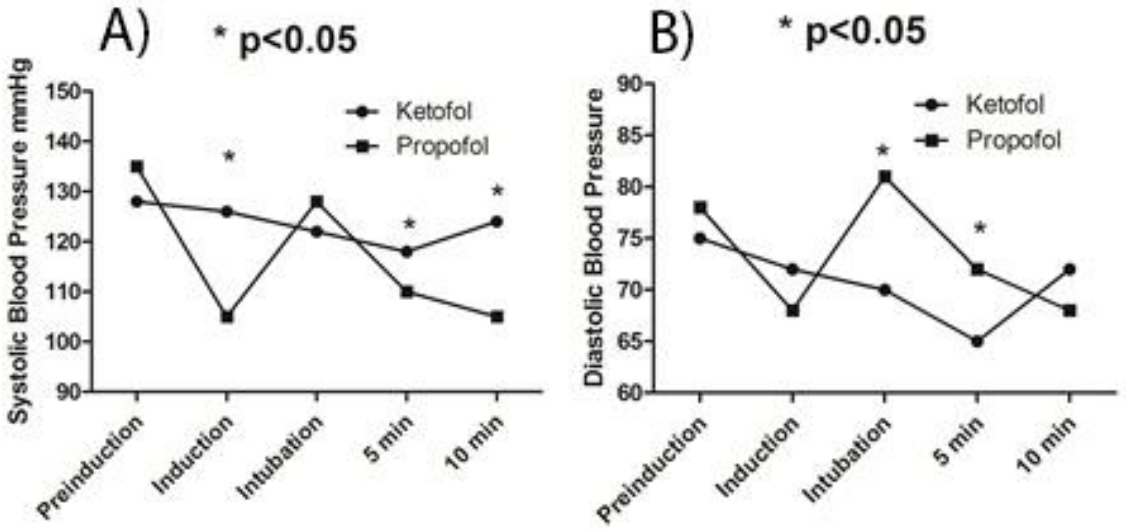

Figure 2. Systolic and diastolic blood pressure in ketofol compare to propofol group.

laparotomy were randomly assigned to one of groups of study. Age, sex, and weight of patients were not significantly different between two groups (Table1).

Heart rate was compared between two groups of study. Heart rate was significantly lower in the propofol group compared to ketofol group at induction (p=0.001) and 5 minutes (p=0.001), and 10 minutes (p=0.001) after intubation. Heart rate was not significantly higher in propofol group compared to ketofol after intubation (p=0.062) (Figure1).

Systolic blood pressure was significantly lower in propofol group compared to ketofol group after induction (p=0.001) and after 5 minutes (p=0.017) and 10 minutes (p=0.002) after intubation. Although systolic BP was higher after intubation in propofol group compare to ketofol but this difference was not significant (p=0.24) (Figure2).

Diastolic blood pressure was lower after induction in propofol group compared to the ketofol group (p=0.054). It was significantly higher in propofol compared to ketofol group at intubation time (p=0.001), 5 minutes after intubation (p=0.001). However, at 10 minutes after intubation, diastolic blood pressure was lower in propofol group compared to ketofol group that was not significant (p=0.10) (Figure 2).

Mean arterial blood pressure (MAP) was significantly lower in propofol group compared to ketofol group at the induction time (p=0.001). At intubation time MAP was significantly higher in propofol group compared to ketofol (p=0.014). MAP was significantly lower in propofol group compared to ketofol at 5 minutes (p=0.015) and 10 minutes (p=0.022) after intubation.

Discussion

In this study, we compared effect of ketofol and propofol on patients underwent elective laparotomy for their hemodynamic changes during induction, intubation and post-intubation time. Our results depicted that ketofol not propofol stabilized hemodynamics during induction, intubation and post-intubation time. Ketofol has a significant effect on the trend of systolic, diastolic, mean blood pressure, and heart rate.

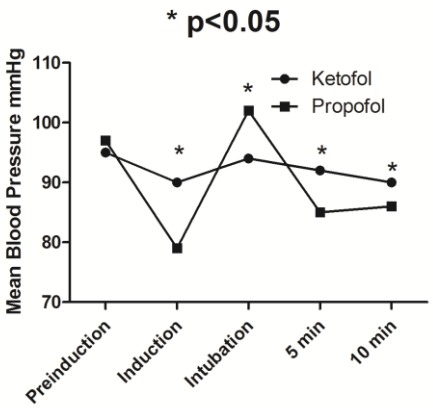

Figure 3. Mean arterial blood pressure in ketofol compare to propofol group.

One of the major challenges in anesthesia is to maintain hemodynamic in a predictable and controlled range during induction and intubation and then the incision of surgery. Ketofol, a combination of ketamin and propofol could maintain hemodynamic during induction, intubation and surgical incision particularly in patients prone to sudden drop or increase in hemodynamic. In a systematic review, ketofol was effective in reducing cardiovascular complications (8). A case series describes the use of the ketofol as an induction agent for intubation in critically ill patients when hemodynamic stability is desired (9). There was no difference between propofol+ketamine versus propofol+etomidate in mean arterial pressure (MAP) and heart rate (HR) during induction of anesthesia in elderly patients (10). Ketofol is a safe and effective induction agent for LMA insertion in children with rapid onset of action and improved hemodynamic stability with less prolonged apnea when compared with propofol (11). Recent reports showed that the number of patients in need of ephedrine was significantly lower and SBP immediately and in 5 min. after PLMA insertion was significantly higher in the ketofol group compared to the propofol group (12). Ketofol improves hemodynamics when compared to addition of fentanyl to propofol, and is associated with better LMA insertion conditions (13).

Mechanism of ketamine by inhibition of afferent pain, sensory inputs and decrease in spinothalamic transmission decrease stimulation of sympathetic responses to pain stimulation including blood pressure and heart rate. Ketamine is rapidly distributed and absorbed into the brain. Ketamine metabolism is in the liver and its elimination half life is 2-3 hours.

Intubation induces disturbances in hemodynamic responses. Propofol decreases hemodynamic variables, including blood pressure and heart rate. Ketofol does not decrease these variables in patients due to blocking severe hemodynamic disturbances and inhibition of sympathetic reactivation in response to pain.

Skin incision appears somewhat in the middle of noxious stimuli, being more stimulating than electrical pain, but much less stimulating than laryngoscopy and intubation (14). The depth of anesthesia is of paramount importance in clinical responses to noxious stimuli. In our study the depth of anesthesia was kept at the BIS:40-60 which is defined as appropriate for depth of anesthesia not-responding to noxious stimuli. Suppressing the most refractory response, hypertension and tachycardia, to the most profound stimulus, intubation, requires yet more opioid and hypnotic. Ketofol seems to suppress pain sensation and decrease the hemodynamic responses better than propofol alone. This potentially could decrease the need for increasing the opioid dose.

Ketofol has its main impact on trend of blood pressure (both systolic and diastolic) and heart rate. This trend follows a stable pattern after induction

Table 1: Demographic characteristics

	Ketofol (n=48)	Propofol (n=48)	p-value
Weight	65.5	67.2	0.3
Age	39.7	36.3	0.4
Sex (Male/Female)	23/22	25/20	0.3

through intubation and in post-intubation time. Such stable trend is probably due to decrease in sympathetic stimulation by somatic pain stimulatory input. This implies the fact that a major barrier to hemodynamic stability is the over-activation of sympathetic nervous system.

Conclusion

Ketofol is a proper alternative to propofol to stabilize heart rate and blood pressure in laparotomy.

Acknowledgment

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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