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Comparison the Effects of Propofol and Ketofol on Sedation in ICU Patients with CABG Surgery

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Abstract

Objective: We investigated the effects of propofol and ketofol on sedation in ICU patients with CABG surgery.

Design: A randomized double-blind clinical trial study.

Setting: Afshar hospital, Shahid Sadoughi University of medical sciences, Yazd, Iran.

Patients or Subjects: Ninety patients with ASA class 1, 2 aged 40 to 60 years old, underwent CABG surgery, were involved.

Interventions: Patients were categorized in Ketofol (n=45) or propofol (n=45) group .All patients underwent general anesthesia using a same protocol. After the surgery, patients were transferred to ICU. In propofol group, patients' sedation was maintained with propofol at dose of 15mic/kg/min. In ketofol group, in addition to propofol at dose of 15mic/kg/min, ketamine was added at dose of 3mic/kg/min.

Measurements and Main Results: Patient's pain was measured every 2 hours using Behavioral Pain Scale. During patient's ICU stay, MAP and HR were measured and recorded in both groups. Comparing two groups in terms of heart rate, significant differences were found merely at time points of 0.5, 1 and 2.5 hours after ICU admission in a way that heart rate was lower in Ketofol group. The mean of arterial blood pressure was significantly higher in ketofol group 4 and 5 hours following ICU admission. Based on RASS scores, patients' sedation was -0.93 ± 0.252 in ketofol group and -1.24 ± 0.435 in propofol group that was statistically significant (P.value = 0/001) . Based on Behavioral Pain Scale scores, there was no significant difference in mean pain intensity in different times between two groups.

Conclusions: Optimal sedation and analgesia in ICU patients can be achieved by using ketofol during intubation following CABG surgery.

Keywords: Propofol; Ketofol; Sedation; CABG

Introduction

Sedation following open heart surgery has a special importance for anesthesiologists and cardiac surgeons since preferably the patient should be gently awaken to reduce the pressure on the heart. Mostly, patients need analgesics in addition to sedation to bear intubation, experience more natural sleep process, and have more balanced response to physiological stress (tachycardia and hypertension) [1,2]. Sources of pain after cardiac surgery include the sternotomy incision, chest tubes, and leg incision. Pain increases sympathetic tone and can result in tachycardia and hypertension, increases pulmonary vascular resistance and the oxygen consumption. Pain after heart surgery also has negative effects on the respiratory system. Inadequate sedation can increase morbidity and mortality in ICU patients. To achieve the goals mentioned in the ICU, it is tried to use sedative and analgesic separately, or in combination [3-6]. Propofol is commonly used in the ICU as a sedative and in comparison with other drugs it can create an effective sedation with appropriate and immediate recovery; moreover, extubation is done faster and less analgesic is required by using propofol [7]. Ketamine is a drug that can induce appropriate amnesia and analgesia and can maintain airway muscle tone and spontaneous breathing. Since propofol has no significant analgesic effect, it seems that combination of these two drugs can create effective sedation and analgesia. Various studies reported the efficacy of these two drugs combination in inducing effective sedation and

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maintaining appropriate hemodynamic. In addition, cardiovascular effects of both drugs are opposite each other; that is, ketamine can prevent decrease of mean Arterial blood Pressure (MAP) and Cardiac indices. The comparison of propofol with ketofol (propofol and ketamine combination) has been conducted in several studies [8-10]; however, no study has yet considered patients undergoing CABG surgery and admitted to the ICU. In this study, we investigated the efficacy of these two protocols with respect to sedative, analgesic, and hemodynamic effects on patients hospitalized in ICU following CABG surgery.

Materials and Methods

After approval by ethics committee and obtaining informed written consent, in this randomized double-blind clinical trial study, 90 patients with ASA class 1, 2 aged 40 to 60 years old, underwent CABG surgery, were involved. Patients were excluded if they need IABP and inotropic drugs, have impaired renal function tests, have EF <40%, or if they have to be hospitalized in ICU more than 24 hours. Moreover, addicted patients, patients with known psychiatric problems and history of seizures were not involved for the current study. Patients were categorized in two groups (45 patients in each group), including Ketofol or propofol group using random number table. All patients underwent general anesthesia using a same protocol. After the surgery, patients were transferred to ICU. In propofol group, patients' sedation was maintained with propofol at dose of 15mic/kg/min. In ketofol group, in addition to propofol at dose of 15mic/kg/min, ketamine was added at dose of 3mic/kg/min (with ratio of 1 to 5). It should be noted that sedative drugs were prepared by anesthesia technicians and were delivered to ICU nurse for patient's sedation. The quality of patient's sedation examined the using Richmond criteria. Patient's pain was measured every two hours using Behavioral Pain Scale. If PBS> 5, 3 to 5mg of morphine was administered every ten minutes to obtain PBS <5. The maximum dose of morphine was set as 20mg. Delirium was assessed according to CAM-ICU criteria following patient's extubation. In the case of delirium, 2.5-5 mg of haloperidol was given every 6 hours. During patient's ICU stay, MAP and HR were measured and recorded in both groups; that is, every 30 minutes in the first 4 hours and then every hour up to patient's extubation. To analyze the data, SPSS (version 19) was used. Mean and standard deviation were used for analysis of quantitative data and independent *t* test was run to compare the groups. P <0.05 considered significant.

Results

In this randomized, double-blind clinical trial, 90 patients with ASA class 1 and 2 aged between 40 to 60 years old and underwent CABG surgery, were evaluated. There was no significant difference between two groups in terms of sex (P.value=0/490). The mean age, BMI, and EF were not significantly different in two groups and two groups had been matched well. Comparing two groups in terms of heart rate, significant differences were found merely at time points of 0.5, 1 and 2.5 hours after ICU admission in a way that heart rate was lower in Ketofol group (Table 1). The mean of arterial blood pressure was significantly higher in ketofol group 4 and 5 hours following ICU admission (Table 2). The amount of morphine consumption and duration of intubation were significantly lower in ketofol group. Although the amount of propofol consumption was lower in ketofol group, this difference was not statistically significant (Table 3). Based on RASS scores, patients' sedation was -0.93 ± 0.252 in ketofol group and -1.24 ± 0.435 in propofol group that was statistically significant (P.value = 0/001) (Table 4). Based on Behavioral Pain Scale scores, there was no significant difference in mean pain intensity in different times between two groups (Table 5). The prevalence of delirium was 6.7% in ketofol group and 0% in propofol group but it was not statistically significant (P.value = 0.078).

Table 1: Mean heart rate in different times between two groups.

Time	mean heart rate (beat/min)		p.value
	ketofol	propofol	
30 minutes after ICU admission	79.16	84.89	0.001
1 hour after ICU admission	79.84	86.58	0.009
1.30 hours after ICU admission	81.93	87.02	0.061
2 hours after ICU admission	82.11	86.44	0.088
2.30 hours after ICU admission	81.6	89.33	0.005
3 hours after ICU admission	85.6	87.18	0.46
3.30 hours after ICU admission	86.18	86.42	0.908
4 hours after ICU admission	87.91	89.78	0.512
5 hours after ICU admission	86.97	92.2	0.076
6 hours after ICU admission	90.78	92.4	0.099

Table 2: Mean arterial blood pressure in different times between two groups.

Time	mean arterial blood pressure (mm/Hg)		p.value
	ketofol	propofol	
30 minutes after ICU admission	75.09	72.22	0.364
1 hour after ICU admission	77.7	80.16	0.447
1.30 hours after ICU admission	80.93	79.99	0.788
2 hours after ICU admission	84.81	86.47	0.541
2.30 hours after ICU admission	80.74	79.93	0.805
3 hours after ICU admission	80.88	77.95	0.338
3.30 hours after ICU admission	84.44	81.53	0.238
4 hours after ICU admission	79.26	73.96	0.053
5 hours after ICU admission	80.79	72.32	0.002
6 hours after ICU admission	86.12	80.75	0.126

Table 3: Mean morphine consumption, propofol consumption and duration of intubation between two groups.

Variables	propofol	ketofol	p.value
Morphine consumption (mg)	14.44	9.67	0.01
Propofol consumption (µg)	596.67	572.73	0.38
Duration of intubation (hour)	6.93	5.42	0.004

Table 4: Mean RASS score between two groups.

Time	propofol	ketofol	p.value
2 hours after ICU admission	3.80-	3.76-	0.808
4 hours after ICU admission	3.20-	2.91-	0.092
6 hours after ICU admission	1.24-	0.93-	0.001

Discussion

After heart surgery, patients are intubated and need to wake up gently. In addition to sedation, other anesthetics are needed for intubation tolerance and creation of analgesia, more natural sleep process, and more balanced response to physiological stress, including tachycardia and hypertension [1,2]. To achieve these goals, sedatives

Table 5: Mean pain intensity according Pain Scale Behavioral score between two groups.

Time	propofol	ketofol	p.value
2 hours after ICU admission	13.6	13.71	0.869
4 hours after ICU admission	13.91	13.34	0.403
6 hours after ICU admission	14.29	13.1	0.108

or anesthetics, or combination of both are attempted in ICU [3-6]. Propofol and ketofol are known as sedatives and anesthetics [8-10]. However, these medications can cause some side effects; for instance, propofol may decrease blood pressure and heart rate while ketamine can increase them. In this study, we investigated the efficacy of these two protocols with respect to sedative, analgesic, and hemodynamic effects on patients hospitalized in ICU following CABG surgery.

Bykal et al. compared the effect of propofol with ketofol regarding hemodynamic changes in 96 patients underwent colonoscopy. They concluded that blood pressure and heart rate are lower in propofol group than ketofol [3]. Bykal et al. study is consistent with the current study just in terms of blood pressure but not heart rate. Pilips et al. also investigated the effects of propofol and ketofol on sedation. They stated that ketofol provides less hypotension and better sedation compared to propofol [11], that is consistent with our study. In this study, sedation was compared in two groups using RASS and better sedation was seen in ketofol group. The sedation in propofol group was too deep that can be due to consumption of more morphine in this group and the findings are in line with Pilips's study. Andolfatta et al. compared the effect of propofol and ketofol on sedation of patients who were hospitalized in emergency ward and underwent different procedures. In contrast to present study, they concluded that the depth of sedation in ketofol group was higher than that of propofol group [8]. This lack of correlation can be attributed to this fact that Andolfatta et al. prepared ketofol using 1:1 ratio for ketamine and propofol while we combined ketamine and propofol in 1:5 ratio. That is, the amount of ketamine used in their study was much higher than our study. Urio is not in line with our study either [12]. The results of our study demonstrated that morphine consumption was significantly lower in ketofol group compared to propofol group. Since the presence of ketamine in ketofol combination can create appropriate analgesia and propofol do not have significant analgesic effect [8,9]. It seems that the combination of these drugs can induce appropriate sedation and analgesia. In this study, the duration of intubation was significantly shorter in ketofol group than propofol group. Because the sedation of patients in ketofol group was lower than those in propofol group and more morphine was consumed by propofol group for intubation tolerance and analgesia creation, longer duration of intubation in propofol group can be justified.

Conclusion

According to the current study, an optimal sedation and analgesia in ICU patients can be achieved by using ketofol during intubation following CABG surgery.

Acknowledgment

*Authors have no conflicts of interest.

*Study protocol was in accordance with the latest Declaration of Helsinki for medical research involving human subjects and was approved by local ethics committee.

*This article does not contain any studies with animals performed by any of the authors.

*Informed consent was obtained from all participants of the study.

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