RESEARCH ARTICLE

Effect of Different Doses of Remifentanil on Hemodynamic Profiles and Intubation Conditions in Patients Undergoing Coronary Artery Bypass Graft Surgery, a Randomized Double-Blinded Placebo Controlled Trial

Sohrab Salimi[1], Morteza Jabbari Moghaddam[1], Noushin Khazaei[1], Ali Movafegh[2], Omid Azimaraghi[2], Reza Atef Yekta[2], Alireza Saliminia[2], Seyed Sajjad Razavi[3]*

Background: Hemodynamic instability is common during tracheal intubation. The primary purpose of the present study is to evaluate the effect of different doses of remifentanil added to propofol on the hemodynamic profiles during tracheal intubation.

Methods: Ninety patients, 40 to 70 years old, undergoing coronary artery bypass graft surgery under general anesthesia were randomly allocated into control, low (2µg/kg) and high (4ug/kg) dose groups. Baseline heart rate (HR), mean arterial pressure (MAP) were recorded and documented again on intubation and 1, 2 and 4 minutes after intubation. Cough status before and after intubation was also recorded.

Results: The basic characteristics of participants in all the three groups were similar. Heart rate and blood pressure decreased in all three groups after intubation. There was no difference in the intubation conditions and mask ventilation or coughing between the three groups.

Conclusion: There was no significant difference observed between hemodynamic changes with high and low dose of remifentanil to attenuate the rise in MAP on intubation.

Keywords: remifentanil; tracheal intubation, cardiovascular response

During induction of general anesthesia and tracheal intubation many adverse reactions such as hemodynamic changes and coughing can be evoked. These adverse events could lead to irreversible complications especially in patients with a history of hypertension or ischemic heart disease; therefore it is of great importance to every anesthesiologist to experience a smooth intubation with the least evoked response of the hemodynamic reflexes. Various techniques such as deep intubation, intravenous administration of opioids, beta blockers or intravenous and local lidocaine prior to intubation have been studied previously, however, each of them have showed some limitations and they have not shown consistent results [1-3].

Remifentanil, an ultra-short acting opioid has a short context sensitive half time. Previously the efficacy of this drug on adverse reaction of emergence of anesthesia has been studied [4-5]. The primary purpose of the present study is to evaluate the effect of different doses of remifentanil added to propofol on hemodynamic profiles during intubation in patients undergoing coronary artery bypass graft surgery. Effect of different doses of remifentanil on intubation conditions in patients undergoing coronary artery bypass graft surgery were considered as secondary outcomes.

Methods

An informed written form of consent was obtained from the patients. The study protocol was approved by the institutional ethics committee. A total number of 90 patients were randomly selected from the patients whom had been candidate for elective coronary artery bypass graft surgery under general anesthesia. Adults aged between 40 to 70 years of old compliant with American Society of Anesthesiologist physical status (ASA) II and III, were enrolled in the study.

The exclusion criteria consisted of patients with a history of upper respiratory tract hyper reactivity, asthma or any other respiratory related diseases. Patients with a history of previous laryngeal or tracheal surgery or pathology, and those whom were under treatment with sedatives, antitussives, or angiotensin converting enzyme inhibitors were also excluded from the study. Smokers and addicts

From the [1]Department of Anesthesiology and Critical Care, Emam Hussain Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
[2]Department of Anesthesiology and Critical Care, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.
[3]Department of Anesthesiology and Critical Care, Mofid Hospital, Shahid Beheshti Medical University, Tehran, Iran
Received: 7 June 2016, Revised: 25 June 2016, Accepted: 11 July 2016
The authors declare no conflicts of interest.
*Corresponding author: Seyed Sajjad Razavi, MD. Department of Anesthesiology and Critical Care, Mofid Hospital, Shahid Beheshti Medical University, Tehran, Iran. E-mail: s.razavi@sbmu.ac.ir

(including opioids and benzodiazepines), were also excluded from the study.

Prior to general anesthesia all the required drugs were prepared by an anesthetist who was not involved in the administration or observation of the patient; thus, both the anesthesiologist and the patients were blinded to group assignment. Using a computer-generated randomization list, patients were randomly assigned into three groups; control (group C, n=30), low dose group (group L, n=30), and high dose group (group H, n=30). On arrival in operating room, all patients were monitored with an electrocardiogram (ECG), noninvasive blood pressure and pulse oximetry. An 18-gauge cannula was inserted and lactated ringer solution 7 ml/kg was administered.

In group L anesthesia was induced with remifentanil (2 ug/kg) and propofol (1.5 mg/kg). In group H anesthesia was induced using remifentanil (4ug/kg) and propofol (1.5 mg/kg). The trachea was intubated one minute after induction of anesthesia. No muscle relaxant was administered in groups L and H. In group C anesthesia was induced using thiopental sodium and sufentanil and endotracheal intubation was facilitated with 0.5 mg/kg atracurium and the trachea was intubated after three minutes. After tracheal intubation, anesthesia was maintained by isoflurane. Ventilation was adjusted to maintain normocapnia (end-tidal carbon dioxide partial pressure 4.7-5.3 kPa).

Baseline heart rate (HR), and mean arterial pressure (MAP) were recorded. Variables recorded at the baseline were noted down again on intubation, and 1, 2 and 4 minutes after intubation. Cough was defined as an abrupt noisily expulsion of air from the lungs plus a strong contraction of the abdomen.

The incidence of coughing during and after intubation was recorded. The intubation conditions faced by the anesthesiologist were scaled as easy, medium and difficult and were recorded down.

Statistical analysis of the results was performed using SPSS for windows, release 13.5 (SPSS. Inc). The distribution of data was evaluated by the Kolmogorov-Smirnov test. They followed a normal distribution. For statistical analysis of demographic data and comparison of different groups one way ANOVA was used. Fischer's exact or Chi-square tests were appropriate for analysis of categorical data. HR and MAP were analyzed by repeated measurement analysis. Two tailed P-values<0.05 were considered statistically significant.

Results

Ninety patients met the inclusion criteria and were enrolled in the study. Thirty patients were in the control group (group C) who received sufentanil and thiopental sodium and atracurium and 30 cases in each of the other two groups who received remifentanil 2ug/kg (group L) and remifentanil 4ug/kg (group H) with 1.5 mg/kg propofol without neuromuscular blocking agents.

The basic characteristics of the participants were similar in all three groups and are presented in table 1. Changes in heart rate and mean arterial pressure are presented in table 2. Changes seen in between the three groups was not statistically significant.

The incidence of coughing during intubation was 13.3% in group H and 43.3% in L group in comparison to 3.3% in group C which was statistically significant. There was no statistically significant difference between patient movement or facemask ventilation during intubation in between the three groups. Anesthesiologist faced difficult intubating conditions in 3 patients in each of the interventional groups compared to one in the control group.

Table 1- Basic characteristics and baseline parameters of the participants

Variables	Group L	Group H	Group C	P value
Age(years)	59±10.6	60±8.6	59±9.2	0.23
Weight(Kg)	71±13.1	68±13.3	69±.52	0.59
Baseline Mean arterial pressure	102±22	102±23	110±25	0.18
Baseline Heart rate	73±18	80±20.2	82±9.8	0.78

Table 2- Changes in heart rate and mean arterial pressure after intubation in all groups

Tracheal Intubation	1 min before	1 min after	2min after	4min after	P value
MAP					
Group L	102±22	62±21	57±18	64±19	0.13
Group H	102±23	66±23	63±22	63±20	0.25
Group C	110±25	59±22	55±22	58±21	0.37
HR					
Group L	73±18	61±12	58±12	56±11	0.16
Group H	80±20	67±16	64±16	62±15	0.19
Group C	82±9	65±14	64±13	59±14	0.47

Discussion

In this study the effect of low dose and high dose remifentanil added to propofol, on hemodynamic profiles after tracheal intubation of patients undergoing CABG surgery was studied. This study illustrated that both high and low dose of remifentanil lead to a stable hemodynamic profile following tracheal intubation. There were no statistically differences in hemodynamic profiles of patients who received high or low doses of remifentanil.

The drop in MAP observed after intubation with thiopental sodium and sufentanil, although not statistically significant, but clinically, it was unfavorable. The fact that no considerable difference was observed between patients receiving high dose and low dose remifentanil supports using low dose remifentanil. It's reasonable to suggest that

low dose remifentanil may be more relevant in preventing changes in hemodynamics in patients undergoing CABG compared to high dose remifentanil.

Although the hemodynamic profile was satisfactory with different doses of remifentanil and propofol, the intubating condition was not as good as it was expected to be, with much higher incidence of coughing during induction of anesthesia after the use of remifentanil and propofol compared to when neuromuscular blocking drugs where used. Previously it was shown that intravenous magnesium sulphate effectively attenuated both heart rate and arterial blood pressure responses to laryngoscopy and intubation compared with intravenous lignocaine [6]. It has also been previously shown that small bolus doses of remifentanil can attenuate the hemodynamic responses to intubation [7].

Combination of remifentanil and propofol without muscle relaxants compared to rocuronium with propofol and remifentanil has been shown to accompany a poorer intubating condition although the dose of muscle relaxant needed when used in concomitantly with remifentanil and propofol is less [8]. It has been proposed to add a low dose of muscle relaxant before induction of anesthesia using remifentanil and propofol to optimize the intubating conditions in addition to the hemodynamic profile [9-13]. This condition may be more promising especially in outpatient surgery where using muscle relaxant is not welcomed especially in the pediatric population [13-15].

The main shortcoming of this study apart from a small number of patients studied, was that serum levels of remifentanil was not measured between the studied groups which may be required when studying different doses of drugs and their effects. We suggest that in future studies, dose titration of remifentanil on hemodynamic profiles following sternotomy, which causes a great instability, be studied.

In conclusion, both 2ug/kg and 4ug/kg of remifentanil added to propofol attenuate the hemodynamic response to laryngoscopy during induction of anesthesia in patients undergoing CABG surgery.

References

1. Mort TC. Complications of emergency tracheal intubation: hemodynamic alterations-Part I. J Intensive Care Med. 2007; 22(3):157-65.
2. Shrestha M, Rahman TR, Agarwal B. Hemodynamic changes during endotracheal intubation: A prospective randomised comparative study using fibreoptic bronchoscope and intubating laryngeal mask airway. Journal of Society of Anesthesiologists of Nepal. 2014; 1(2):70-5.
3. Hassani V, Movassaghi G, Goodarzi V, Safari S. Comparison of fentanyl and fentanyl plus lidocaine on attenuation of hemodynamic responses to tracheal intubation in controlled hypertensive patients undergoing general anesthesia. Anesth Pain Med. 2013; 2(3):115-8.
4. Guignard B, Menigaux C, Dupont X, Fletcher D, Chauvin M. The effect of remifentanil on the bispectral index change and hemodynamic responses after orotracheal intubation. Anesth Analg. 2000; 90(1):161-7.
5. Tuzcu K, Tuzcu EA, Karcioglu M, Davarci I, Coskun M, Ilhan O, et al. The Effects of Remifentanil and Esmolol on Increase in Intraocular Pressure Due to Laryngoscopy and Tracheal Intubation: A Double-Blind, Randomized Clinical Trial. J Glaucoma. 2015; 24(5):372-6.
6. Sunil R, Vijay S, Jerry P. The role of intravenous magnesium sulphate in attenuating pressor response to laryngoscopy and intubation in patients undergoing major head and neck surgeries. Ain-Shams Journal of Anaesthesiology. 2014; 7(3):451-5.
7. Zhang GH, Sun L. Peri-intubation hemodynamic changes during low dose fentanyl, remifentanil and sufentanil combined with etomidate for anesthetic induction. Chin Med J (Engl). 2009; 122(19):2330-4.
8. Schlaich N, Mertzlufft F, Soltesz S, Fuchs-Buder T. Remifentanil and propofol without muscle relaxants or with different doses of rocuronium for tracheal intubation in outpatient anaesthesia. Acta Anaesthesiol Scand. 2000; 44(6):720-6.
9. Barclay K, Eggers K, Asai T. Low-dose rocuronium improves conditions for tracheal intubation after induction of anaesthesia with propofol and alfentanil. Br J Anaesth. 1997; 78(1):92-4.
10. Stevens JB, Wheatley L. Tracheal intubation in ambulatory surgery patients: using remifentanil and propofol without muscle relaxants. Anesth Analg. 1998; 86(1):45-9.
11. Grant S, Noble S, Woods A, Murdoch J, Davidson A. Assessment of intubating conditions in adults after induction with propofol and varying doses of remifentanil. Br J Anaesth. 1998; 81(4):540-3.
12. Klemola UM, Mennander S, Saarnivaara L. Tracheal intubation without the use of muscle relaxants: remifentanil or alfentanil in combination with propofol. Acta Anaesthesiol Scand. 2000; 44(4):465-9.
13. Alexander R, Olufolabi AJ, Booth J, El-Moalem HE, Glass PS. Dosing study of remifentanil and propofol for tracheal intubation without the use of muscle relaxants. Anaesthesia. 1999; 54(11):1037-40.
14. Geldner G, Wulf H. Muscle relaxants suitable for day case surgery. Eur J Anaesthesiol Suppl. 2001; 23:43-6.
15. Meakin GH. Muscle relaxants in paediatric day case surgery. Eur J Anaesthesiol Suppl. 2001; 23:47-52.