The Effect of Low-Dose Remifentanil on the Hemodynamic Responses of Endotracheal Extubation

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Abstract- Emergence from general anesthesia can be associated with coughing, agitation, and hemodynamic disturbances. Remifentanil may attenuate these responses. We have examined the effect of remifentanil on the hemodynamic response to the emergence from anesthesia and tracheal extubation. In a double-blind, randomized trial, we enrolled 50 adult patients undergoing abdominal surgery. All patients received a standard general anesthetic comprising propofol, atracurium and 1% isoflurane with 50% nitrous oxide in oxygen. At the end of surgery, a bolus dose of remifentanil 0.2 microgram/kg (n = 25) or saline placebo (n = 25) was given and tracheal extubation was performed when standard criteria were achieved. Arterial pressure and heart rate were measured non-invasively, immediately after tracheal extubation and then at 1-min intervals. Remifentanil attenuated the increase in both systolic and diastolic arterial pressure and heart rate after extubation compared to the control group. No differences in SpO2, cough and laryngospasm were observed between two groups. Use of a low-dose remifentanil has clinically acceptable effect in blunting the cardiovascular changes induced by tracheal extubation.

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Introduction

The purpose of tracheal intubation is to provide airway patency, ensuring airway protection, to aid ventilation of the lungs and improving surgical access. The endotracheal tube could be withdrawn, when there is no further need to ventilatory assistance and/or protection of the airways (1). Despite the enormous attention granted to tracheal intubation, especially about the management of the difficult airway (2), little attention has been paid to tracheal extubation and its challenges (3). In most patients, extubation is uneventful. However, in a some cases, anatomical and/or physiological problems, technical and human factors can result in morbidity and mortality which occur more commonly among high-risk patients (1).

The period immediately after extubation is considered as most critical and vulnerable time for the patient that, it is highly recommended for anesthesiologists by American Society of Anesthesiologists (ASA), to have a preplanned strategy for management of potential problems after extubation (3-4). In addition to respiratory complications, hemodynamic complications such as hypertension, increasing intraocular and intracranial pressure, tachycardia, and dysrhythmia can occur with extubation that can be hazardous in high-risk patient (4-5).

Some pharmacological agents have been used to attenuate the cardiovascular and respiratory changes associated with extubation, including opioids, calcium channel antagonists, magnesium, lidocaine, clonidine, ketamine and beta-blockers (6).

Remifentanil is an opioid with instant effect and rapid elimination that is not influenced by age or the functions of the liver and kidneys, and does not result in delayed recovery or respiratory depression after a continuous infusion and recently it has been recommended as a promising agent in attenuating hemodynamic and respiratory complications of anesthesia (7). The aim of this study was to assess the effects of low-dose Remifentanil injection on the hemodynamic responses of extubation.

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Materials and Methods

This study was conducted with the approval of the Scientific & Ethical Review Boards of Urmia University of Medical Sciences. After obtaining written informed consent, 50 patients between the ages of 20-50 years who were scheduled for abdominal surgery, were enrolled in our double-blinded clinical trial. All patients were ASA physical status I-II according to the ASA's classification system. Subjects were randomly assigned into two groups (case and control) using a computer-generated table of random numbers. Patients under long-term treatment with sedatives, antitussives, or angiotensin converting enzyme inhibitors, patients with chronic cough, asthma, or predicted difficult intubation were excluded from the study. Preoperative evaluation was performed in all patients. Before the induction of anesthesia, all patients received 5ml/kg serum ringer to maintain intravascular volume and were premedicated with intravenous 2 µg/kg of fentanyl and 0.015mg/kg of Midazolam. Anesthesia was induced using 2mg/kg intravenous propofol. Atracurium 0.6 mg/kg was administrated to facilitate intubation. Maintenance was with inhalant 1% isoflurane, atracurium, fentanyl and nitrous oxide in oxygen (50:50). Patients were monitored during surgery. At the end of surgery, all the patients received fentanyl 1 µg/kg and after discontinuing isoflurane and N2O, we used the combination of atropine and prostigmine to antagonize the remaining effects of non-depolarizing neuromuscular blocking agents and mechanical ventilation was continued with 100% oxygen. In this time, oropharyngeal suction was preformed genteelly, and then the extubation was considered in a standard manner when the patients were able to open their eyes and squeeze hands on command. When the patients obtained the extubation criteria two minutes before extubation, 1mg/kg of 1% lidocaine was administrated for all patients and 90 second prior to extubation, the case group received bolus 0.2 µg/kg intravenous remifentanil whilst the control group received similar amount of saline solution as placebo. A blinded observer measured blood pressures, heart rate, the oxygen saturation (SpO_2), cough, and the occurrence of laryngospasm in minute 1-6 after extubation. Data were analyzed via chi-square and independent t-tests, or Fisher's exact & Mann-Whiteny U tests where needed, using SPSS statistical software ver16 (Chicago, IL).

Results

In this randomized, double-blind trial, 50 ASA I-II patients between the ages 20-50 years were enrolled. All patients were extubated, when they were awake. The mean age was 39.4 ± 6.7 years in case group and 36.8 ± 6.9 years in the control group. There was no significant age difference between two groups (P=0.17). In the case group, 10 (40%) were man and 15 (60%) were woman, 14 patients (56%) in control group were man and 11 (44%) were woman (P=0.25).

Mean basic systolic pressure (SBP) before Remifentanil injection was 156.4 ± 24.6 mmHg in case group and 158.42 ± 26.13 mmHg in the control group (P=0.3). The mean basic diastolic pressure (DBP) was 91.58 ± 12.8 mmHg in case group and 92.16 ± 11.49 mmHg in control group (P=0.2).

Significant difference was observed between SBP & DBPs of two groups in minute 1, 2, 3 after extubation. In minute 4, DBPs were statistically different but there was no significant difference in mean SBPs. No significant difference was observed between the SBPs & DBPs of two groups in minute 5 & 6 after extubation (Table 1).

Table 1. Baseline patients' characteristics

Characteristics	Remifentanil group	Control group	*P*-value
Age (Mean±SD)	39.4 ± 6.7	36.8 ± 6.9	0.17
Sex (Male/Female)	10/15	14/11	0.25
Baseline SBP (mmHg)	156.4 ± 24.60	158.42 ± 26.13	0.3
Baseline DBP (mmHg)	91.58 ± 12.80	92.16 ± 11.49	0.2
Baseline HR (beats/min)	100.36 ± 13.25	101.62 ± 16.71	0.3

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate

The mean heart rates (HR) and blood oxygen saturation (Spo2) before and in minute 1, 2, 3, 4, 5, 6 after extubation were demonstrated and compared between two groups in Table 2 as well. Cough was reported in 4 patients (16%) vs. 6 patients (24%) in minute 1 (P=0.7), one patient (4%) and 2 patients (8%) in minute 2 (P=0.5) after extubation, respectively in remifentanil and Saline groups. Only one patient from

remifentanil group had cough in the 3rd minute (*P*=0.3). Cough was not observed in 4th & 5th minutes post-extubation, but 3 patients from the Saline group reported having cough in minute 6 after extubation (*P*=0.7). Only one patient from the control group was reported to experience the laryngospasm in the 1st minute after extubation, and no laryngospasm was reported in the subsequent minutes in any of groups.

Table 2. The findings of 1st, 2nd, 3rd, 4th, 5th, 6th minute after extubation in two groups

		Remifentanil group	Control group	*P*-value
SBP (mmHg)	1 min	140.04 ± 28.80	160.48 ± 28.15	0.01*
	2 min	137.08 ± 25.48	161.54 ± 29.93	0.003*
	3 min	133.44 ± 26.44	148.52 ± 19.47	0.02*
	4 min	130.12 ± 23.99	137.76 ± 19.94	0.2
	5 min	127.00 ± 21.18	126.48 ± 23.86	0.9
	6 min	126.16 ± 21.46	126.12 ± 24.95	0.1
DBP (mmHg)	1 min	83.68 ± 13.80	93.16 ± 11.49	0.001*
	2 min	82.24 ± 15.21	94.58 ± 12.29	0.003*
	3 min	79.88 ± 15.87	89.44 ± 10.72	0.01*
	4 min	79.88 ± 15.87	89.44 ± 10.72	0.04*
	5 min	76.8 ± 13.56	80.24 ± 11.76	0.3
	6 min	75.32 ± 12.01	80.16 ± 13.59	0.1
HR (beats/min)	1 min	86.36 ± 14.30	102.72 ± 17.81	0.001*
	2 min	84.28 ± 14.13	101.00 ± 16.93	0.001*
	3 min	83.24 ± 12.35	96.28 ± 18.51	0.005*
	4 min	80.96 ± 12.71	90.60 ± 15.43	0.02*
	5 min	79.24 ± 13.73	87.76 ± 18.76	0.07
	6 min	85.56 ± 11.77	86.12 ± 17.69	0.2
SaO2 (%)	1 min	97.76 ± 4.70	97.32 ± 4.40	0.7
	2 min	97.72 ± 3.14	97.96 ± 1.76	0.7
	3 min	97.36 ± 3.20	97. 55± 2.1	0.3
	4 min	97.80 ± 1.90	98.00 ± 1.20	0.6
	5 min	97.56 ± 1.90	97.96 ± 1.20	0.3
	6 min	97.80 ± 1.90	98.16 ± 1.20	0.4

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; SaO2: Oxygen Saturation; *: Statistically significant (P<0.05)

Discussion

Extubation is uneventful in most patients, but in some cases, anatomical and/or physiological problems, technical and human factors can result in morbidity and mortality, especially in high-risk patients (1). Thomson and Hall found remifentanil as an effective agent in hemodynamic stabilization during intubation and anesthesia (8-9). Whilst there are several studies about effects of remifentanil on hemodynamic changes during intubation, fewer studies have been dedicated to assessing its effects on hemodynamic changes after extubation process. In our study, there was no bradycardia or hypotension associated with Remifentanil, which was reported in some of the previous studies. Lack of these findings can be attributed to the administration of Atropine and Neostigmine in our study that was not performed in previous studies.

The result of our study showed that administration of 0.2 µg/kg remifentanil before extubation can prevent the increase in SBP, DBP and HR after extubation.

In the study of Aouad *et al.,* remifentanil administration was associated with slower heart rates and lower incidence of cough during extubation in patients who underwent nasal surgery, and also in the study of Lee, Remifentanil significantly reduced post-extubation coughing, in patients who underwent thyroidectomy (10-11). In our study, systolic and diastolic blood pressures and heart rates were significantly lower in the remifentanil group, whilst there was no significant difference in the incidence of cough between two groups. This result can strongly suggest that the incidence and severity of cough is well depended on the type of surgery and remifentanil is more effective in cough reduction in oronasal surgeries, in which blood discharge can stimulate cough reflex.

Wu et al assessed the efficacy and safety of low-dose remifentanil for attenuating cardiovascular response to tracheal extubation (12). They (Wu et al.,) reported that remifentanil at the optimal dose of 0.10 µg/kg (-1) min (-1) can effectively prevent cardiovascular response (change of systolic and diastolic blood pressure and heart rate) to tracheal extubation and reduce the adverse effect associated with anesthesia without prolonging the recovery time. Nho *et al.*, also found similar results in their study (13). Shajar *et al*., reported in their trial that remifentanil attenuated both mean arterial pressure and heart rate during extubation and there was not a

significant difference in time to recovery from anesthesia or in time to discharge from the recovery room in (remifentanil vs control) groups (14). In the study of Nishina administration of 1-2 µg/kg remifentanil attenuated cardiovascular changes during extubation in patients who underwent gynecologic surgery and it did not prolong the recovery (15). In present study, Oxygen saturation levels never decreased to less than 97% in neither of two groups and it can be attributed to low frequency of cough and lack of laryngospasm which itself is probably related to the type of surgery. Considering the findings of this study in association with the literature, the administration of 0.20 µg/kg bolus remifentanil before extubation, seems to be effective in reducing hemodynamic responses after extubation. As mentioned above, Remifentanil has an instant effect and rapid elimination, and does not result in delayed recovery, so it can be used in different types of surgery and in critically ill patients for whom hemodynamic changes can be challenging.

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