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Administration of Remifentanil in Establishing a more Stable Post-anesthesia Cardiovascular Status in Neurosurgical Procedures

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ABSTRACT

Introduction*:** Emergence from general anesthesia and especially post-extubation phase are the stages associated with cardiovascular hyperdynamic status in which patients with increased intracranial pressure (ICP) could be affected by severe cardiac and or cerebral complications. Administering remifentanil could be helpful in maintaining the hemodynamic stability at the end of the surgery and recovery stages and reducing recovery phase length. ***Methods*:** In a double-blind prospective randomized clinical trial, 60 adult patients with ASA (American Society of Anesthesiologist) class of I-II scheduled to undergo elective neurosurgery operations were randomly divided into two groups receiving remifentanil and placebo as IV infusion within four minutes prior to extubation continued by an IV infusion for 10 minutes after extubation. ***Results*:** There was a significant difference between two groups regarding the changes of Mean Arterial Pressure after extubation and five minutes after extubation ($P< 0.001$).Remifentanil group compared with control group was of significant difference at all heart rate values after extubation ($P< 0.001$).Conclusion*:** Remifentanil could be used in preventing hyperdynamic status throughout extubation phase without extending recovery phase length. However, administration of this medication should be performed cautiously.

Introduction

Emergence from general anesthesia and especially post-extubation phase are the stages associated with cardiovascular hyperdynamic status leading to increase in oxygen consumption, catecholamine release and pain. Post-operative pain can be derived from the anesthesia techniques used for the surgery, for instance, the back pain caused following spinal anesthesia or the surgical process solely.[1,2] This phase lasting 15 to 5 minutes could frequently be accompanied by tachycardia and hypertension.[3] Most patients however could endure this temporary encountered situation appropriately.[4] On the other hand, patients having preoperative hypertension and cardiovascular and cerebrovascular diseases and patients with increased intracranial pressure (ICP) could be affected by severe cardiac and or cerebral complications.[5] Therefore, it is of great importance to prevent postoperative and post intubation sympathetic excitations in high-risk patients as maintaining stability in the dynamic status reduces the mortality and morbidity rates in these patients.[3] Remifentanil hydrochloride is a recent μ agonist receptor which is being reported to be associated with better hemodynamic stability under surgical stress conditions compared with other narcotics such as fentanyl [6,7] or alfentanil.[8] Remifentanil could be associated with low to moderate hypotension.[9] Considering the fact that pain is one of the major factors contributing to sympathetic excitement at the end of the surgery and recovery stages, we aimed at evaluating the efficacy of pre-extubation administration of remifentanil on maintaining the hemodynamic stability at the end of the surgery and recovery stages and its effects on recovery phase length.

Materials and methods

This study is a double-blind prospective placebo-control randomized clinical trial which was carried out after obtaining approval of the ethics committee of medicine

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faculty, Tabriz University of Medical Sciences and informed written consents from the patients. 60 adult patients with ASA (American Society of Anesthesiologist) class of I-II which were scheduled to undergo elective neurosurgery operations were randomly divided into two groups. Exclusion criteria from the study included pregnant females, patients with heart rate less than 60, systolic blood pressure less than 100 mmHg, considerable hepatic, renal or cardiovascular complications. All patients were premeditated with fentanyl (2µg/kg IV) and lidocaine (1.5 mg/kg IV) and intubated using Sodium Thiopental (7-5 mg/kg) and Cisatracurium (0.15 mg/kg). Anesthesia was maintained using Isoflurane(1-1.5%) and a mixture of O2(50%) and N2O (50%). Mechanical ventilation was maintained with a tidal volume of 10 mL/kg and at a rate to keep End-tidal CO2 at the range of 35-30 mmHg. Repeated doses of Cisatracurium (0.05 mg/kg) were used to provide intraoperative muscle relaxation. Administration of anesthetics was terminated when suturing the skin and muscle relaxation was antagonized with neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg) after reestablishment of spontaneous breathing.

Remifentanil group: in this group IV infusion of remifentanil (0.2 mg/kg) was administered within four minutes prior to extubation continued by an IV infusion of remifentanil at the rate of 0.1 mg/kg/min for 10 minutes after extubation.

Control group: in this group IV infusion of normal saline (0.5 ml/kg) was administered within four minutes prior to extubation continued by an IV infusion of normal saline at the rate of 0.15ml/kg/min for 10 minutes after extubation.

Medications were prepared and coded previously by a colleague so that the coworker performing the records was unaware of the contents of the syringes. All patients were given IV lidocaine (1.5 mg/kg) 90 seconds prior to extubation. Systolic and diastolic blood pressure, mean arterial pressure and heart rate were recorded before and after medication administration and extubation. Vital signs were recorded every five minutes at recovery phase until the patient was discharged from the recovery unit. Time required for performing eye opening to verbal commands, spontaneous eye opening and recognition of the location and people at the recovery unit were recorded for both groups.

All studied data were analyzed using statistical software SPSS16. To evaluate the statistics, descriptive statistical approaches (frequency, percentage, mean and standard deviation) were used. To compare qualitative variables, Chi-square statistical test and to compare quantitative variables in paired groups, independent-test was used. The changes in quantitative findings throughout the study in groups were evaluated using repeated measure of ANOVA. P <0.05 was considered significant in this study.

Results

Table 1 presents the demographic findings between two groups. As it can be seen, demographic findings are equal in two groups and no statistically significant difference is observed (P> 0.05).

Table 1. Demographic findings between two groups

	Control group	Remifentanil group	P
Age (Year)	49.03±17.00	43.62±15.83	0.26
Sex (M/F)	9/21	16/14	0.14
Weight (Kg)	71.57±12.02	66.82±11.08	0.15
Operation duration (Minutes)	186.56±62.65	193.27±38.80	0.73
ASA (II/I)	16/14	11/19	0.39

The changes in the levels of systolic blood pressure (SBP) were statistically significant at all values of SBP at all studied stages following extubation (All P<0.05) (Table 2).

Table 2. Changes in Systolic Blood Pressure (mmHg) between two groups

	Control group	Remifentanil group	P
Before extubation	115.63 ± 14.93	104.86 ± 15.83	0.01
After extubation (immediate)	137.86 ± 21.10	109.80 ± 15.12	<0.001
After extubation (5 minutes)	134.36 ± 21.94	110.53 ± 18.99	<0.001
After extubation (10 minutes)	132.43 ± 24.09	109.93 ± 17.20	<0.001
After extubation (15 minutes)	125.81 ± 17.21	110.50 ± 14.30	0.001

The study of the changes in diastolic blood pressure (DBP) in two groups revealed a significant difference at all values of SBP after all studied stages following extubation (All P<0.05; Table 3). The changes in heart rate in two groups are presented in Table 4. A significant difference was observed between two groups at all stages (P< 0.05).Dysrhythmia was not reported in any of the groups.

Comparing both groups regarding the levels of arterial oxygen saturation (SaO2) at different stages revealed that there was a significant difference regarding SaO2levels between remifentanil and control groups after extubation(P= 0.03) and five minutes after extubation(P= 0.001).The mean of recovery phase and extubation duration for two groups have been presented in Table 5. A significant difference regarding extubation phase length can be observed between remifentanil and

control groups ($P< 0.001$). However, the differences in recovery phase are not significant; confirming the fact that remifentanil does not prolong the recovery phase significantly.

Table 3.Changes in Diastolic Blood Pressure (mmHg) between two groups

	Control group	Remifentanil group	P
Before extubation	71.90 ± 13.09	80.93 ± 16.26	0.58
After extubation (immediate)	85.13 ± 15.85	67.70 ± 13.65	<0.001
After extubation (5 minutes)	85.56 ± 18.92	68.23 ± 13.92	<0.001
After extubation (10 minutes)	84.33 ± 23.64	68.70 ± 13.94	0.003
After extubation (15 minutes)	76.59 ± 12.68	69.66 ± 13.48	0.05

Table 4. Changes in Heart Rate (bpm) between two groups

	Control group	Remifentanil group	P
Before extubation	77.56±12.54	71.00±12.24	0.04
After extubation (immediate)	91.13±12.96	71.63±14.13	<0.001
After extubation (5 minutes)	89.60±15.30	69.23±11.59	<0.001
After extubation (10 minutes)	83.96±12.33	70.30±12.05	<0.001
After extubation (15 minutes)	81.51±10.62	70.33±12.20	0.001

Table 5. The mean of extubation and recovery phase length between two groups (minutes)

	Control group	Remifentanil group	P
Extubation	4.60±1.73	7.86 ± 2.82	<0.001
Eye opening with verbal commands	12.60±3.37	12.80 ± 3.12	0.81
Spontaneous eye opening	16.30±4.51	16.56 ± 3.48	0.79
Orientation	21.16±6.10	21.36 ± 4.99	0.89

Discussion

Patients with hypertension and cardiovascular or cerebrovascular diseases and patients with increased ICP could accompany severe cardiac and or cerebral complications at extubation phase.[4,7] Therefore, managing hemodynamic responses such as heart rate and blood pressure while disconnecting from mechanical ventilation would be of great importance.

Numerous strategies have been introduced to prevent hemodynamic responses caused by emergence from anesthesia including extubation under deep anesthesia, administration of local anesthetics, vasodilators and short acting opioids.[9,10]

One of the most frequently used medication groups is opioids. In modern anesthesia, mostly to prevent a hyperdynamic cardiovascular status followed by tracheal intubation fentanyl is used.[11] In a study carried out by Nishina *et al.*, fentanyl was introduced to prevent hyperdynamic cardiovascular status followed by extubation.[12] In the present study, we selected remifentanil because of its short acting characteristic which would not prolong recovery phase. Different studies have concluded that remifentanil, compared with other opioids including fentanyl and alfentanil, is accompanied with a more stable hemodynamic status under surgical stress.[7,13] The results obtained from the present study revealed that Remifentanil could be administered to prevent hemodynamic instability caused by extubation. It has previously been proven that hyperdynamic cardiovascular status caused by sympathetic excitation followed by extubation could endure for 5 to 10 minutes.[1] Considering the fact that remifentanil is of very short half-life, in addition to administration of a bolus does before extubation, we used IV infusion of remifentanil within 10 minutes after extubation which was associated with desirable results. In a similar study carried out by Parish *et al.* hemodynamic changes reported to be more frequent in the control group compared with the remifentanil group.[14] In the present study, remifentanil group had a longer extubation time compared with the control group which could be explained by the dose-dependent respiratory suppression effect of opioids. However, Nho *et al.* observed no significant difference between two groups of remifentanil and control regarding the length of extubation time [15] which could have been due to genetic differences.

An appropriate anesthetic for neurosurgery should provide the possibility of early evaluation of the neurologic status of the patients and early diagnosis of the potential postoperative complications (for instance; hematoma and major cerebral edema) by a rapid and short recovery phase.[15,16] In the present study, there was no significant difference between both groups regarding the time of eye opening (to verbal commands and spontaneous) and the recovery phase length. In the study of Nho *et al.* also the most significant difference between two groups of remifentanil and control was observed regarding the time of eye opening and discharge from recovery unit.[16] Shajar *et al.* also reported no significant change in the recovery phase length followed by administration of a bolus dose of remifentanil.[17]

Conclusion

Sympathetic excitation followed by extubation would lead to increase in MAP and HR and therefore the patients at risk of cardiovascular and cerebral complications should be prevented from these excitations. Remifentanil could be used in preventing hyperdynamic status throughout extubation phase without extending recovery phase length. However, due to more frequent respiratory suppression and prolonged extubation observed in remifentanil group, administration of this medication should be performed cautiously.

Recommendations

Based on the results obtained from the present study, it could be advised to administer remifentanil in cases in which more aggressive control of hemodynamic status is required in high-risk patients undergoing intracranial surgeries. A combination of medications with more balanced doses would probably be associated with more favorable results; therefore, further studies with larger sample sizes to achieve more accurate results are required.

Conflict of interests: The authors declare no conflicts of interest

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