کارگاه‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله
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.

Keywords: Remifentanil, Recovery, Cardiovascular Stability

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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 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 assigned into two groups. Group A received remifentanil (5 μg/kg) and group B received placebo as IV infusion within four minutes prior to extubation continued by an IV infusion for 10 minutes after extubation. The primary endpoint of this study was changes of Mean Arterial Pressure (MAP) after extubation and MAP five minutes after extubation. The secondary endpoints were heart rate (HR) and system arterial pressure (SAP) changes after extubation. Data were analyzed using SPSS 16.0 software. 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.
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 premedicated 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

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Remifentanil group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before extubation</td>
<td>71.90 ± 13.09</td>
<td>80.93 ± 16.26</td>
<td>0.58</td>
</tr>
<tr>
<td>After extubation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(immediate)</td>
<td>85.13 ± 15.85</td>
<td>67.70 ± 13.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(5 minutes)</td>
<td>85.56 ± 18.92</td>
<td>68.23 ± 13.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(10 minutes)</td>
<td>84.33 ± 23.64</td>
<td>68.70 ± 13.94</td>
<td>0.003</td>
</tr>
<tr>
<td>(15 minutes)</td>
<td>76.59 ± 12.68</td>
<td>69.66 ± 13.48</td>
<td>0.05</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Remifentanil group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before extubation</td>
<td>77.56±12.54</td>
<td>71.00±12.24</td>
<td>0.04</td>
</tr>
<tr>
<td>After extubation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(immediate)</td>
<td>91.13±12.96</td>
<td>71.63±14.13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(5 minutes)</td>
<td>89.60±15.30</td>
<td>69.23±11.59</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(10 minutes)</td>
<td>83.96±12.33</td>
<td>70.30±12.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(15 minutes)</td>
<td>81.51±10.62</td>
<td>70.33±12.20</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Remifentanil group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extubation</td>
<td>4.60±1.73</td>
<td>7.86 ± 2.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Eye opening with verbal commands</td>
<td>12.60±3.37</td>
<td>12.80 ± 3.12</td>
<td>0.81</td>
</tr>
<tr>
<td>Spontaneous eye opening</td>
<td>16.30±4.51</td>
<td>16.56 ± 3.48</td>
<td>0.79</td>
</tr>
<tr>
<td>Orientation</td>
<td>21.16±6.30</td>
<td>21.36 ± 4.99</td>
<td>0.89</td>
</tr>
</tbody>
</table>

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. 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. 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. In a study carried out by Nishina et al., fentanyl was introduced to prevent hyperdynamic cardiovascular status followed by extubation. 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. 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. 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. 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 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. 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. Shajar et al. also reported no significant change in the recovery phase length followed by administration of a bolus dose of remifentanil.

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

**References**


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