Comparison in Effect of Intravenous Alfentanil and Lidocaine on Airway-Circulatory Reflexes during Extubation

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Abstract: This randomized controlled double-blind trial was designed to compare the presence of Airway-Circulatory Reflexes to tracheal extubation in groups administering IV alfentanil or lidocaine, in 150 patients undergoing cesarean surgery receiving a standardized anesthetic protocol. At the end of surgery, after return of spontaneous ventilation, patients received either alfentanil 15 μg kg⁻¹ or lidocaine 1.5 mg kg⁻¹. The presence of cough and its severity during emergence before extubation was noted. BP and HR were recorded at 2 min after end of surgery (baseline), 2 min after study drug administration and 1 min after extubation. The groups were matched according to age, baseline BP and HR. The incidence of coughing was less frequent in the alfentanil than in the lidocaine group (19% versus 75%, respectively, p<0.001). Although the severity of coughing was considerably different between two groups (lower in alfentanil g) but was not statistically different (p = 0.292). The mean BP and HR were lower in alfentanil than lidocaine group 2 min after administration and 1 min after extubation (p<0.001). The median of delay time (time between the study drug administration and extubation) was 6 min in alfentanil (Range: 4-8) and 5 min in lidocaine groups (Range: 4-8) (p<0.001). These results indicate that alfentanil decreases Airway-Circulatory Reflexes more than lidocaine during emergence from anesthesia without clinically important prolonging the time to extubation.

Key words: Airway, circulatory reflexes, alfentanil, lidocaine, coughing

INTRODUCTION

The incidence of coughing on emergence from general anesthesia in the presence of an endotracheal tube has been estimated as ranging between 38 and 96% (Minogue et al., 2004; Estebe et al., 2002).

Coughing on emergence can result in a number of undesirable side effects including hypertension, tachycardia, tachyarrhythmias, increased intracranial pressure and increased intraocular pressure (Minogue et al., 2004). Various methods have been applied to attenuate this response, including tracheal extubation while the patient is in a deep plane of anesthesia and IV administration of various drugs, such as lidocaine and short-acting opioids, before tracheal extubation (Minogue et al., 2004; Shajar et al., 1999). Concerns about the use of these techniques include precipitation of airway obstruction, aspiration in the presence of an unprotected airway and delayed emergence from anesthesia.

The efficacy of IV alfentanil and lidocaine in preventing Airway-Circulatory Reflexes on emergence are known but which one can better attenuate these reflexes is unknown and this model study has not been investigated. This randomized controlled double-blind trial was designed to compare the presence of Airway-Circulatory Reflexes to tracheal extubation in groups administering IV alfentanil or lidocaine, in patients undergoing cesarean surgery.

MATERIALS AND METHODS

After institutional approval and obtaining informed consent, 150 healthy patients with ASA physical status I-II, aged 18-35 year scheduled for cesarean section under general anesthesia in Dr Ali Shariati Hospital 2007 were included in this study. Patients with a history of respiratory disease or recent respiratory tract infection, previous laryngeal or tracheal surgery or pathology, coronary artery disease, hypertension, cigarette smoking, opioid addiction, local anesthetic allergy and those taking cardiovascular medications were excluded from the study.

After establishing IV access and routine monitors, patients were breathed with 100% oxygen. All patients received a standardized anesthetic protocol. Anesthesia was induced with thiopental sodium 5 mg kg⁻¹.

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Succinylcholine 1.5 mg kg⁻¹ was then given to facilitate endotracheal intubation. After direct laryngoscopy the trachea was intubated using a standard oral cuffed endotracheal tube 7 mm ID high volume/low pressure (Rüsch Uruguay, Authorized by Rüsch Gmbh, Germany) and the cuff was inflated with a volume of air 2 mL more than that required to prevent a leak with positive pressure ventilation. The lungs were mechanically ventilated using a tidal volume of 8-10 mL kg⁻¹ and the respiratory rate was adjusted to maintain normocarbia. Anesthesia was maintained using isoflurane (1 MAC before neonate birth and 0.5 MAC after neonate birth) in oxygen and 50% nitrous oxide. Muscle paralysis was maintained with atracurium. Immediately after neonate birth IV morphine 0.1 mg kg⁻¹ was administered.

At the end of the surgery, the oropharynx was suctioned, isoflurane and nitrous oxide were discontinued and the patient was administered 100% oxygen. Patients were then placed in the recovery position, mechanical ventilation was discontinued and ventilation was assisted until spontaneous ventilation resumed. Using a randomly generated computer assignment, patients were allocated to receive either 15 μg kg⁻¹ IV alfentanil or 1.5 mg kg⁻¹ IV 2% lidocaine. After return of spontaneous ventilation study drug was administered. After 2 min residual neuromuscular block was reversed using 0.05 mg kg⁻¹ neostigmine and 0.02 mg kg⁻¹ atropine. The trachea was extubated when patients demonstrated the ability to follow verbal commands or had purposeful movement in addition to resumption of regular spontaneous respiration. Systolic BP (SBP), diastolic BP (DBP) and heart rate (HR) were measured 2 min after end of surgery and served as baseline values. Subsequent measurements were taken 2 min after study drug administration (immediately before reverse of neuromuscular block) and 1 min after extubation then compared with baseline values.

A blinded observer noted the presence or absence of cough during emergence before extubation. Cough was recorded as either yes or no. If cough was present, it was graded using a three-category scale (Table 1).

Delay time (defined as the time between the study drug administration and extubation) was recorded.

A sample size of 75 in each group would be sufficient to detect a difference of 25% between them in the coughing rate during emergence before extubation, with 85% power and a 5% significance level. Statistical analysis was performed using statistical package for social sciences (SPSS version 11.5). Distribution was checked by Kolmogorov-Smirnov test. Statistical comparison was carried out by t-test, Mann-Whitney U-test and Chi-square test where appropriate. Repeated measures ANOVA was used to compare Within-Subjects and Between-Subjects effects. Two tailed p<0.05 was taken as significant.

RESULTS

No patients were excluded from the study. The patient characteristics and the duration of surgery were similar in the two groups (Table 2). No patients experienced laryngospasm or bronchospasm after extubation in the two groups.

Incidence of coughing was statistically different between two groups which in lidocaine group 56 cases (74.7%) and in alfentanil group 14 cases (18.7%) had coughing (p<0.001). Although the severity of coughing was considerably different between two groups, it was not statistically different (p = 0.292) (Table 3). Measurement of hemodynamic variables 2 min after end of surgery (baseline), were similar between two groups (Table 4). The measured hemodynamic variables 2 min after administration of study drug and 1 min after extubation were statistically different between two groups and the mean of the variables (SBP, DBP, HR) were higher in lidocaine compared to the alfentanil group (p<0.001) (Table 4). Variation of mentioned variables were statistically different within two groups (Test of within subjects effect; p<0.05) (Table 4). The range of delay time was 4-8 min in each group and median time was 6 min in the alfentanil group and 5 min in the lidocaine group which was statistically different (p<0.001).

Table 1: Three-category scale for scoring cough on emergence

<table>
<thead>
<tr>
<th>Severity</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Mild</td>
<td>Single cough</td>
</tr>
<tr>
<td>Moderate</td>
<td>More than one episode of unassisted (≤5 s) coughing</td>
</tr>
<tr>
<td>Severe</td>
<td>Sustained ≥5 s bout(s) of coughing</td>
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</tbody>
</table>

Table 2: Comparative patient characteristics

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Lidocaine group</th>
<th>Alfentanil group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>28.4±14.9</td>
<td>28.6±14.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>77.9±10.3</td>
<td>80.1±9.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>150.6±12.1</td>
<td>153.4±10.8</td>
</tr>
<tr>
<td>Gestation (week)</td>
<td>39.0±0.1</td>
<td>39.0±0.2</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>58.0±11</td>
<td>60.0±13</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD; There are no significant differences between groups.

Table 3: Severity of coughing during emergence from anesthesia before extubation

<table>
<thead>
<tr>
<th>Severity of coughing</th>
<th>Lidocaine group</th>
<th>Alfentanil group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>28(41.1)</td>
<td>96(64.3)</td>
</tr>
<tr>
<td>Moderate</td>
<td>25(44.6)</td>
<td>4(28.6)</td>
</tr>
<tr>
<td>Severe</td>
<td>8(14.3)</td>
<td>1(7.1)</td>
</tr>
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p = 0.292
Table 4: Comparison of hemodynamic changes between and within groups at different time intervals

<table>
<thead>
<tr>
<th>Hemodynamic variable</th>
<th>Lidocaine group (n = 75)</th>
<th>Alfentanil group (n = 75)</th>
<th>p-value</th>
<th>Lidocaine group (n = 75)</th>
<th>Alfentanil group (n = 75)</th>
<th>p-value</th>
<th>Lidocaine group (n = 75)</th>
<th>Alfentanil group (n = 75)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>122.5±14.7</td>
<td>123.9±11.1</td>
<td>0.449</td>
<td>136.5±14.8</td>
<td>113.5±14.3</td>
<td>0.001</td>
<td>137.3±14.5</td>
<td>126.0±13.2</td>
<td>0.001</td>
</tr>
<tr>
<td>DBP</td>
<td>77.3±8.5</td>
<td>78.1±8.7</td>
<td>0.057</td>
<td>88.2±15.0</td>
<td>65.8±12.4</td>
<td>0.001</td>
<td>83.3±13.2</td>
<td>75.5±12.2</td>
<td>0.001</td>
</tr>
<tr>
<td>HR</td>
<td>94.7±16.3</td>
<td>96.8±14.0</td>
<td>0.397</td>
<td>101.5±16.4</td>
<td>76.2±14.9</td>
<td>0.001</td>
<td>120.1±16.1</td>
<td>109.7±15.0</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; HR = Heart Rate

**DISCUSSION**

In the present study, we found that the Airway-Circulatory Reflexes on emergence from anesthesia were less frequent in the alfentanil group than in the lidocaine group.

The occurrence of Coughing during emergence from anesthesia varies greatly and has been estimated to occur in up to 96% of patients (Minoque et al., 2004; Estebe et al., 2002). The stress reaction coupled with coughing may not only cause hypertension and tachycardia, but can also induce bronchospasm in patients with hyperactive airways (Irwin, 2006). The increased intracranial, intracranial and intra-abdominal pressure can lead to surgical complications such as bleeding or severe injury (Hohlrieder et al., 2007). Moreover, coughing has the potential to dislodge peripheral and central venous catheters through uncontrolled patient movement (Diachun et al., 2001). As the depth of anesthesia decreases after discontinuing anesthetic agents, the probability of coughing occurrence increases as the tracheal tube exerts a constant laryngotracheal stimulation. Thus, standardization of the measurement time point is of particular importance when determining cough frequency. In contrast to the induction of anesthesia, where it is possible, for example using Bispectral Index (BIS) monitoring, to aim for a particular depth of anesthesia that would reliably prevent intubation stress and coughing (Heck et al., 2000), there exists no comparable monitoring procedure for the wake-up phase.

In order to ensure identical study conditions in both groups, we set the exubation and measurement time point in all patients according to generally recognized clinical parameters of the awake state (the ability to follow verbal commands or had purposeful movement in addition to resumption of regular spontaneous respiration). Previous studies have investigated various techniques and medications to prevent coughing during emergence. Neither extubation in a deep plane of anesthesia (Neelakanta and Miller, 1994) nor the use of the laryngeal mask airway (Koga et al., 1998) is generally applicable in patients at increased risk of aspiration or with a difficult airway. Techniques involving the topical application of lidocaine (Minoque et al., 2004) bear the risk of blocking airway reflexes and may predispose to aspiration (Hohlrieder et al., 2007). Besides, the endotracheal instillation of fluid may itself induce coughing and agitation. The administration of lidocaine via the tracheal tube requires a modified tube (LITA™) (Diachun et al., 2001) and has not proved to be reliable (Andrzejowski and Francis, 2002). Intra-cuff lidocaine (Fegan et al., 2000) can be dangerous if the cuff ruptures (Estebe et al., 2002).

It is known that intravenously lidocaine may decrease Airway-Circulatory Reflexes on emergence. However, Jee and Park (2003), observed no difference in the incidence of coughing during emergence after administering IV lidocaine (1 mg kg⁻¹) 3 min before extubation. In a study, Jang and Oh (2005) showed that after sevoflurane anesthesia, 1.5 mg kg⁻¹ of IV lidocaine 5 min before extubation did not reduce the incidence of emergence agitation in children.

The effects of opioids on the hemodynamic response to orotracheal intubation have been extensively studied (Hohlrieder et al., 2007), but data on the influence of opioids on coughing during emergence are rare. In a study carried out by Mendel et al. (1995), alfentanil was effective in reducing coughing before extubation after isoflurane anesthesia. Many anesthesiologists believe that the administration of opioids at the end of anesthesia reduces the probability of emergence induced coughing.

In this study, the median of delay time was longer (1 min) in alfentanil group. However, the time at which extubation was possible was delayed after alfentanil, but this delay was not considered clinically important.

In conclusion, this study shows that alfentanil offers the advantage of less coughing and hemodynamic stimulation during emergence from general anesthesia in the cesarean section surgery compared to intravenously lidocaine, without clinically important prolonging the time to extubation.

**REFERENCES**


