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Original contribution

Dose requirements of alfentanil to eliminate autonomic responses during rapid-sequence induction with thiopental 4 mg/kg and rocuronium 0.6 mg/kg☆,☆☆

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Abstract

Study objective: Opioids are integral part of anesthesia induction, but information on optimal dosing is limited. We aimed to determine doses of alfentanil needed to eliminate increases in 5 autonomic response variables (plasma concentrations of epinephrine, norepinephrine and vasopressin, arterial blood pressure [ABP], and heart rate) during rapid-sequence induction of anesthesia with thiopental 4 mg/kg and rocuronium 0.6 mg/kg.

Design: Prospective, randomized, observer-blinded, interventional clinical study.

Setting: Large academic institution.

Patients: Eighty-four healthy patients, aged 18 to 55 years, received 1 of 7 assessor-blinded doses of alfentanil (0, 10, 20, 30, 40, 50, and 60 μg/kg) together with thiopental 4 mg/kg and rocuronium 0.6 mg/kg, administered in rapid succession (15 seconds). Laryngoscopy was initiated 40 seconds after rocuronium, and tracheal intubation was concluded within 15 seconds thereafter.

Measurements: An indwelling radial artery catheter was used for hemodynamic monitoring and blood sampling. Relationships between alfentanil dose and response variables were tested with linear regression, and the influence of covariates (sex, body weight, and age) was determined. Alfentanil dose needed to prevent increases in ABP >10% above baseline with 95% probability was estimated with logistic regression.

Main results: Significant relationships were determined between alfentanil dose and response variables. Clinically interesting influence of covariates was not found. Alfentanil 55 μg/kg was needed to prevent increases in ABP postintubation >10% above baseline with 95% probability. One individual needed a bolus of vasopressor postintubation.

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Conclusions: Optimal control of autonomic responses during rapid-sequence induction was achieved with clinically relevant doses of alfentanil in healthy patients anesthetized with thiopental 4 mg/kg and rocuronium 0.6 mg/kg.

1. Introduction

Laryngoscopy and tracheal intubation cause significant release of stress hormones, that is, norepinephrine from cervical sympathetic nerve endings [1-3] and epinephrine and norepinephrine from the adrenal medulla to the blood stream [1]. Vasopressin may also be released from the pituitary gland [2,3]. Opioids attenuate the release of catecholamines secondary to airway manipulation [4], but the efficacy of opioids on the release of stress hormones during rapid-sequence induction and tracheal intubation (RSII) has not been reported. The first primary aim of this investigation was to determine the dose-response relationship between alfentanil and release of catecholamines and vasopressin during RSII with thiopental 4 mg/kg and rocuronium 0.6 mg/kg.

Epinephrine and norepinephrine release caused by laryngoscopy and tracheal intubation is associated with hemodynamic responses [4-12]. Although well tolerated in healthy individuals, increases in arterial blood pressure (ABP) and heart rate (HR) may be harmful in certain groups of patients, that is, patients with cardiovascular or cerebrovascular diseases, intracranial hypertension, and preeclampsia [13,14]. Therefore, during clinical anesthesia, measures must frequently be taken to minimize these physiologic effects of airway stimulation. Alfentanil 30 μg/kg effectively blunted hemodynamic responses to laryngoscopy and tracheal intubation when performed approximately 180 seconds after administration of thiopental 4 mg/kg and suxamethonium 1.5 mg/kg in premedicated elective cases [4]. However, information regarding the efficacy of alfentanil when this procedure is performed in a rapid-sequence fashion is limited. As a second primary aim, we determined dose-effect relationships between alfentanil and hemodynamic responses (ABP and HR) during RSII in patients anesthetized with thiopental 4 mg/kg and rocuronium 0.6 mg/kg and estimated the alfentanil dose sufficient to eliminate these responses in ≥95% patients under such clinical circumstances.

The initial volume of distribution of alfentanil decreases with increasing body weight and is increased in females compared to males [15]. Because men on average are heavier than women, these findings imply that higher blood concentrations of alfentanil are attained in males than females when the drug is administered on a milligrams-per-kilogram basis, potentially modifying responses to airway manipulation differently in the 2 sexes. Therefore, because covariates might influence the magnitude of responses to airway manipulation, we tested if sex, body weight, and age affect the relationships between alfentanil dose and magnitude of autonomic responses (release of stress hormones, ABP, and HR) during RSII.

2. Materials and methods

This study was approved by the Review Board of the Norwegian Committee on Ethics in Human Research (Ethical Committee no. 99042, Region Eastern Norway, Chairperson Professor Knut Engedal, January 21, 2008) and registered with Clinicaltrials.gov (NTC 01518608).

2.1. Enrollment

Study subjects were enrolled between January 2009 and December 2012, and written informed consent was obtained from all participants. Eligible study subjects were American Society of Anesthesiologists class 1 patients with Mallampati airway class 1 or 2, scheduled for elective surgery. Exclusion criteria were as follows: age > 5 or <18 years, body mass index >28 kg/m^2, presence of gastroesophageal reflux, use of medication known to interfere with cardiovascular function, and anticipated difficult airway. Intubation conditions and autonomic responses were simultaneously recorded. The data on intubation conditions have been published previously [16].

2.2. Study population

Eighty-four eligible patients, undergoing gastrointestinal or urological procedures, were randomly allocated using random-number table to receive 1 of 7 different doses of alfentanil (0, 10, 20, 30, 40, 50, or 60 μg/kg). The allocation sequence was concealed from the researchers by using numbered, opaque, and sealed envelopes containing information on the dose of alfentanil to be used. A nurse anesthetists not involved in the study picked the envelope that would be assigned to each study subjects and prepared the drug amount to be administered. The allocation process consequently produced study groups with 12 subjects each. The anesthesia induction procedure was otherwise identical in all study subjects. Demographic data are shown in Table 1.

2.3. Anesthetic technique

Premedication was not given. Anesthesia was induced in rapid-sequence fashion after 3 minutes of preoxygenation, the aim being to have a cuffed endotracheal tube in place within 70 seconds. Cricoid pressure was not applied. Total drug administration time was 15seconds, alfentanil administered first, thiopental second, and rocuronium third. Drugs were injected into an intravenous catheter at the dorsum of the hand, through which NaCl 0.9% was running rapidly.