Original Contribution

The concentration of desflurane preventing spectral entropy change during surgical stimulation: A prospective randomized trial

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ARTICLE INFO

Article history:
Received 23 November 2015
Received in revised form 31 October 2016
Accepted 7 December 2016

Keywords:
Desflurane
Spectral entropy
Surgical stimulation

ABSTRACT

Study objective: To determine the concentration of desflurane necessary to blunt changes in spectral entropy during surgical incision when two different target-controlled effect-site concentrations of remifentanil (1 and 3 ng/ml) were infused.

Design: Prospective, randomized controlled study.

Setting: Operating room of a university hospital.

Interventions: Forty-two patients undergoing general anesthesia for elective surgery were enrolled and randomly allocated to the R1 (1 ng/ml of remifentanil, n = 21) or R3 (3 ng/ml of remifentanil, n = 21) group. After at least a 10-min administration of target-controlled remifentanil concentration and predetermined end-tidal desflurane following endotracheal intubation, changes in spectral entropy in response to surgical incision were evaluated.

Measurements: Concentration of desflurane necessary to blunt changes in spectral entropy during surgical incision for each group was determined using Dixon’s up-and-down method. Hemodynamic variables including mean arterial pressure (MAP) and heart rate (HR) were measured.

Main results: Concentration of desflurane necessary to blunt changes in spectral entropy during surgical incision in 50% of patients (EC50) was 4.1% (95% CI: 3.5-4.7%) for the R1 group and 3.4% (95% CI: 3.0-3.8%) for the R3 group (P = 0.033). Additionally, the calculated EC95 values using the logistic regression analysis for the R1 and R3 groups were 5.8% (95% CI: 5.0-10.8%) and 5.1% (95% CI: 4.3-10.6%), respectively, respectively. MAPs and HRs were significantly higher in the R1 than in the R3 group after surgical incision.

Conclusions: Desflurane 4.1% with remifentanil 1 ng/ml and desflurane 3.4% with remifentanil 3 ng/ml significantly blunt the change in spectral entropy after surgical incision in 50% of patients.

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1. Introduction

General anesthesia consists of amnesia, analgesia, immobility, loss of consciousness, and blunted responses to noxious stimuli [1] and a combination of sedatives and analgesics is required to achieve this state. Insufficient anesthesia or analgesia may lead to intraoperative awareness with recall or pain, whereas anesthetic overdose may be associated with various adverse events [1]. However, there is wide inter-patient variability in the need for hypnosis and analgesia, and therefore, individual and quantitative assessment using objective measures are required to validate anesthetic depth.

Anesthetics result in dose-dependent changes the electroencephalogram (EEG), and EEG-derived devices such as the bispectral index or spectral entropy are used clinically during general anesthesia [2]. The bispectral index suggests the depth of anesthesia by sedatives [3] whereas spectral entropy, measured by a device based on EEG analysis techniques [4], suggests the level of neurological entropy; this value decreases during deep anesthesia [1]. Additionally, frequency domain entropy calculation of spectral entropy can predict EEG responses to stimulation by identifying changes in fast frequencies [1].

The spectral entropy monitor displays state entropy (SE) and response entropy (RE) values with numerical values ranging from 100 (fully awake) to 0 (deepest level of sedation). SE mainly suggests the degree of hypnosis, similar to the bispectral index, and is usually maintained between 40 and 60 during general anesthesia. RE reflects electromyographic (EMG) activity of the facial muscles [5]. The difference between RE and SE can serve as a marker of nociception, and it is
suggested that analgesics are required when the difference between RE and SE is > 10 [5]. Desflurane is a volatile anesthetic with similar pharmacokinetic characteristics to remifentanil [6]. Minimum alveolar concentration (MAC) is used as an index of the potency of inhalation anesthetics needed to prevent patient movement in response to a supramaximal stimulus (traditionally, surgical incision) in 50% of patients [7]. During balanced anesthesia, remifentanil significantly reduces the concentration of desflurane required to prevent sympathetic responses to noxious stimulation such as endotracheal intubation and surgical stimuli [8]. Decola et al. [9] investigated the effect of remifentanil, a potent μ opioid agonist, on MAC-BAR (blocking autonomic response) during surgical incision and showed that 5.2 and 2.2% of desflurane was required with 1 and 3 ng/ml remifentanil, respectively. However, this concentration of desflurane (2.2%) may be associated with intraoperative awareness as this value is close to the MAC-awake value (0.3–0.4 MAC).

The intensity of anesthesia should ideally be estimated before surgical stimulation. In this study, we hypothesized that the proper concentration of desflurane could prevent spectral entropy responses as well as hemodynamic responses to noxious stimuli. Therefore, this prospective and randomized study was conducted to determine the concentration of desflurane necessary to blunt changes in spectral entropy during surgical incision using a modified Dixon’s up-and-down method when two different target-controlled concentrations of remifentanil (1 and 3 ng/ml) were co-infused during surgical stimulation.

2. Materials and methods

After the study was approved by the Institutional Review Board of Kangbuk Samsung Hospital (No. KBC13170) and registered with the Clinical Research Information Service (CRIS, registration number KCT0000898), written informed consent was obtained from each patient. This was performed in Kangbuk Samsung Hospital (Seoul, Republic of Korea) between October and November 2013. This study enrolled 46 patients (ages 31 to 65 years) classified as American Society of Anesthesiology physical status I and II and scheduled for elective surgery requiring at least a 3-cm-long skin incision under general anesthesia. Those with remifentanil hypersensitivity, pregnancy, chronic use of benzodiazepine or opioid drugs, psychiatric medication, or BMI ≥ 30 were excluded from the study. Exclusion criteria after randomization included the administration of vasoconstrictor (mean arterial pressure [MAP] < 50 mmHg) or anticholinergic agents (heart rate [HR] < 45 bpm) before surgical treatment.

![Flow diagram of the patients](image_url)

*Fig. 1. Flow diagram of the patients. Forty six patients were randomized and a total of 42 patients completed the study. One patient in R3 group did not receive intervention because the equipment failure (absence of target controlled infusion). Two patients in the R1 group and one patient in the R3 group were discontinued from the intervention because of the occurrence of hypotension before surgical intervention. R1 group = remifentanil 1 ng/ml group; R3 group = remifentanil 3 ng/ml group.*
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