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BRIEF REPORT

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Bispectral index variations during tracheal suction in mechanically ventilated critically ill patients: effect of an alfentanil bolus

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Abstract *Objective:* To evaluate the impact of an alfentanil dose on bispectral index (BIS) variations during tracheal suction in ICU sedated patients. *Design and setting:* A prospective open-label pilot study in a 12-bed surgical ICU in a university-affiliated, tertiary referral hospital. *Patients*: Eleven sedated (midazolam plus fentanyl) mechanically ventilated patients. *Interventions:* Continuous monitoring of BIS with arterial pressure and heart rate before, during, and after tracheal suction without (control period) and with an intravenous bolus of alfentanil (15 µg/kg, alfentanil period) before suction. *Results:* Steady-state BIS value was 61±8 for the control period and 59±7 for the alfentanil period. Blood pressure and heart rate were similar between baseline periods. One minute after tracheal suction, a significant increase in BIS level was observed in the control period, which remained significantly different from the alfentanil period until 10 min later. Significant higher systolic and diastolic blood pressure and heart rate were observed during the control period than the alfentanil period. However, no difference in Ramsay scores was observed between the two periods. *Conclusions*: An alfentanil bolus of 15 µg/kg markedly reduced the increase in BIS values, blood pressure, and heart rate observed immediately after tracheal suction. Therefore BIS monitoring in ICU may help to improve analgesia during invasive events.

Keywords Bispectral index · Sedation · Alfentanil · Ramsay score · Tracheal suction · Intensive care unit

Introduction

Ensuring adequate sedation and analgesia is an important goal of care of critically ill patients. However, definition and maintenance of "adequate" sedation remain difficult [1]. Of the various sedation scales reported the Ramsay score is the most widely used [2]. Although the Ramsay score may be helpful in detecting oversedation, it does not measure or anticipate pain at all. The analogue visual scale usually used for evaluating pain in the postoperative period is often ineffective in critically ill patients. Nociceptive stimuli are frequently encountered in the routine care of ICU patients, such as nursing, tracheal suction, physiotherapy, and any mobilization [3]. Objective tools to assess the impact of these stimuli on awakeness or analgesia of critically ill patients are scarce.

Electroencephalography (EEG) using the bispectral index (BIS) has recently been developed to monitor depth of anesthesia [4]. BIS is expressed as a value ranging from 0 (plate EEG) to 100 (awake patient). The level of BIS seems to be correlated with the level of hypnosis [4] but not to analgesia. However, clinical studies on both volunteers [5] and anesthetized [6] patients have shown that pain stimulation results in an increase in BIS level if the level of analgesia is weak. Recent investigations have evaluated the value of monitoring sedation in ICU [7, 8]. BIS monitoring could be sensitive to the nociceptive stimuli experienced by critically ill patients.

The aim of the present study was to evaluate the effect of an intravenous bolus of alfentanil on the variations in BIS level associated with tracheal suction, a stimulus often reported as particularly painful by critically ill patients [3].

Patients and methods

Eleven patients hospitalized in a 12-bed tertiary university surgical ICU were included in a prospective pilot study (August 1999–February 2000). The inclusion criterion was mechanical ventilation with intravenous sedation. Exclusion criteria were: (a) renal failure (creatinine clearance <50 ml/min), (b) liver failure (prothrombin time <30% or hepatic encephalopathy), (c) intracranial evolving disease (brain injury, brain tumor, abscess, stroke, or hemorrhage), and (d) patients paralyzed for any reason. The patients comprised eight men and three women, with median age 66 years (range 43–79), weight 72 kg (50–99), height 1.75 m (1.55–1.8), and Simplified Acute Physiology Score 44 (24–64). The MacCabe score was "not fatal" in six patients and "fatal in the next 5 years" in five. The diagnoses on admission were septic shock (n=3), peritonitis (n=2), acute pancreatitis (n=2), and others (n=4).

The sedation protocol was the same for all the patients. This consisted of intravenous midazolam (0.1 mg/kg per hour) and fentanyl (4 µg/kg per hour). The median hourly sedative dose of midazolam was 0.07 mg/kg (0.04–0.16) and that of fentanyl 2.9 µg/kg (1.9–9.7) For the second measurement median alfentanil dose was 14 µg/kg (11–20). Six patients underwent treatment with epinephrine or norepinephrine during the study. The level of sedation was clinically assessed by the Ramsay score, and infusion rates were adjusted to obtain a Ramsay score at 4 or 5 and a BIS level at 60 before the beginning of the protocol. We chose this value because BIS values of 40–65 have been suggested for deep sedation [4] as needed for controlled mechanical ventilation. BIS recording was continuous during the entire study period with an Aspect A-1000 monitor (Aspect Medical System, USA; BIS version 3.03). Four electrodes in a bifrontal schema (F7-Fz; F8-Fz) were used. The impedance of each electrode was checked and maintained below 5000 Ω to ensure a good quality of the signal. Patients' demographic characteristics,, severity score (Simplified Acute Physiology Score II, MacCabe score), and the main diagnosis on admission were recorded.

Each patient served as his own control. The baseline level of BIS before stimulation was recorded during 10 min; then the trachea was suctioned twice for 30 s. Mean baseline BIS was 60±8, without any difference between control and alfentanil for any patient. The BIS level was recorded continuously during the procedure until 15 min after cessation of suction. Fifteen minutes after BIS level returned to baseline an intravenous bolus of alfentanil (15 µg/kg) was administrated 2 min (t_0) before tracheal suction), and the measurement was performed again. For each record of BIS level, systolic (SBP) and diastolic blood pressure (DBP) and heart rate (HR) were noted. Moreover, Ramsay score was evaluated 10 and 5 min before t_0, at t_0, and 5, 10, and 15 min after t_0.

Results are expressed as median with extremes for population data and mean with standard deviation for BIS level, HR (bpm) and SBP and DBP (mmHg). Values during the control period were compared to those during the alfentanil period using the nonparametric paired signed test. The χ^2 test was used to compare qualitative data with Yates' correction or Fisher's exact test, if needed. A P value less than 0.05 was considered significant.

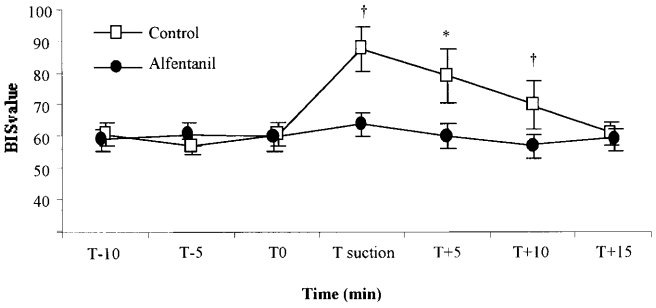

Fig. 1 Comparison of the BIS values (mean ±SD) between the control group and the group receiving an intravenous bolus of alfentanil before tracheal suction according to the protocol. *BIS* Bispectral index. *p<0.01, †p<0.05 between groups

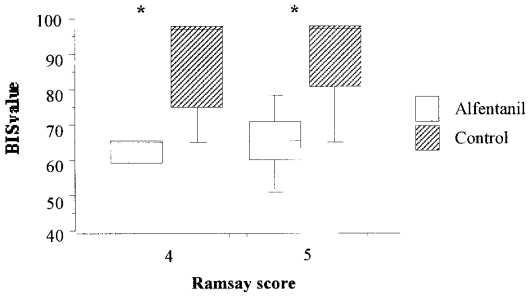

Fig. 2 Comparison between the BIS values (mean ±SD) and the Ramsay score during tracheal suction according to the group receiving or not alfentanil 2 min before. *BIS* Bispectral index. *p<0.05 between groups

Results

BIS variations during the protocol are presented in Fig. 1. Immediately after tracheal suction (integrating time=30 s), BIS values were significantly higher during the control period than the alfentanil period (88±14 vs. 65±9, P=0.02). This difference remained significant 10 min after suction. The pattern of individual variations in BIS according to the period was the same (data not shown). The Ramsay score was 4 or 5 in all patients, without change at any time of the study, even during tracheal suction. The relationship between the Ramsay score observed and the level of BIS is exposed in Fig. 2. No change in the quality of the BIS signal was observed. No patient experienced major coughing during suction. No variation in oxygen saturation was observed. During tracheal suction SBP, DBP, and HR were significantly higher in the control period than after alfentanil bolus: 122±19 vs. 105±20 mmHg (P=0.02), 65±11 vs. 58±11 mmHg (P=0.03), and 100±20 vs. 95±19 bpm (P=0.04). No modification in HR, SBP, and DBP, or BIS values was observed between the bolus of alfentanil and the beginning of the tracheal suction.

Discussion

This study is the first to demonstrate BIS variations during tracheal suction in critically ill patients. These variations were blunted by the administration of an alfentanil bolus before tracheal suction. Together, these results suggest that BIS is sensitive to nociceptive stimuli in critically ill patients.

There are some limitations to our study. First, few patients (n=11) were enrolled, but the size of the sample enabled us to show a statistical difference for the primary end-point (BIS values). Second, each patient was his own control, and a cross-over study was not performed. We did not use randomized control vs. alfentanil periods to avoid a possible persistent effect of alfentanil during the control period if it had been administrated first. Also, a pharmacokinetic/pharmacodynamic simulation was performed before the beginning of the study using Stanpump software. This showed that a period of 2 h was required for alfentanil to be cleared from its site of action in the brain after a bolus of 15 µg/kg. Maintaining hemodynamic and respiratory stability for 2 h is often very difficult in severe ICU patients. Instead of increasing the rate of fentanyl infusion the administration of alfentanil was been chosen owing to its rapid onset of action (threefold faster than fentanyl).

During the control period tracheal suction was rapidly followed by an increase in BIS values This is most likely to be due to a stimulation of central noradrenergic neurons that could realize a kind of "cortical awakeness" [9]. This is supported by the concomitant increase in HR and blood pressure, which reflects adrenergic hyperactivation. This cortical arousal has recently been investigated during tracheal suction in critically ill patients with median nerve somatosensory evoked responses [10]. Therefore it may be suggested that BIS reflects not only the level of hypnosis but also the level of pain. However, the difference between pain-induced cortical arousal or cortical arousal alone without pain is slight. Interestingly, no relationship was found between BIS values and the sedation level assessed by Ramsay score. This apparent discrepancy could be explained by some limitations in sensitivity and specificity of BIS itself [11]. Also, data obtained from a large database of anesthetized patients may not always apply to sedated critically ills [11]. More likely, the Ramsay score measures the depth of sedation but is not sensitive to nociceptive stimuli [2]. Therefore it may not exhibit a good sensitivity to tracheal suction, which is a nociceptive stimulus. Finally, in the present study a Ramsay score of 4 or 5 reflecting deep hypnosis corresponds to BIS values of 60. Although some reports suggest that BIS values and sedation scores may be correlated, our data do not support these findings [7, 8].

In conclusion, this prospective pilot study suggests that BIS variations reflect cortical reactivity to tracheal suction in critically ill sedated and ventilated patients. BIS monitoring in ICU may help to optimize analgesia during invasive events, but this remains to be validated in controlled trials.

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