ORIGINAL ARTICLE

Effect of neuromuscular blockade on the bispectral index in critically ill patients

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Abstract

Introduction: It has been suggested that neuromuscular blockade (NMB) affects the capacity of bispectral index (BIS) monitoring to measure consciousness in sedated children. Our aim was to analyse the impact of NMB on BIS values in critically ill children.

Methods: We conducted a prospective observational study of children monitored with a BIS system that received a continuous infusion of vecuronium. We analysed data on clinical, diagnostic and haemodynamic variables, sedatives, analgesics, muscle relaxants, and BIS parameters. We compared BIS parameters before the use of a muscle relaxant, during its administration, before its discontinuation and for the 24 h following the end of the infusion.

Results: The analysis included 35 patients (median age, 30 months). The most common diagnosis was heart disease (85%). The most frequent indication for initiation of NMB was low cardiac output (45%), followed by adaptation to mechanical ventilation (20%). Neuromuscular blockade did not produce a significant change in BIS values. We found a decrease was observed in electromyography (EMG) values at 6 h (34.9 ± 9.4 vs 31.2 ± 7; P = .008) and 12 h after initiation of NMB (34.9 ± 9.4 vs 28.6 ± 4.8; P = .006). We observed a small significant increase in BIS after discontinuation of NMB (from 42.7 ± 11 to 48.4 ± 14.5, P = .001), and 6 and 12 h later (51.3 ± 16.6; P = .015). There were no differences in the doses of sedatives or analgesics except for fentanyl, of which the dose was lowered after discontinuation of vecuronium.

Conclusion: Continuous NMB produces small changes on BIS values that are not clinically significant and therefore does not interfere with BIS consciousness monitoring in critically ill children.

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Introducción

El índice bispectral (BIS) se utiliza para evaluar la cantidad de sedación en los pacientes. Se determina a partir de la diferenciación de los componentes de los patrones de ondas en el electroencefalograma (EEG). El BIS está diseñado para coexistir con otras técnicas de monitorización. Los datos que aporta se miden de manera continua. El BIS puede usarse para monitorear la profundidad de la anestesia. Las indicaciones para el uso del BIS incluyen la monitorización de los pacientes críticos. Además, el BIS permite comparar la profundidad de la sedación en diferentes pacientes. En este trabajo se presentan los resultados de una investigación prospectiva para evaluar el efecto del bloqueo neuromuscular sobre la monitorización bispectral en niños críticamente enfermos.

Efecto del bloqueo neuromuscular sobre la monitorización bispectral en los niños críticamente enfermos

Resumen

El índice bispectral (BIS) es una herramienta útil para evaluar la sedación en pacientes críticos. El BIS se utiliza para monitorear la profundidad de la anestesia y la sedación en pacientes críticos. Los resultados de esta investigación prospectiva demostraron que el bloqueo neuromuscular disminuye los valores del BIS en niños críticamente enfermos. Específicamente, se observó una disminución en los valores del BIS en niños con tratamiento con bloqueo neuromuscular. Estos resultados sugieren que el BIS es una herramienta útil para monitorizar la sedación en pacientes críticos.

Neuromuscular blockade (NMB) decreases electromyographic activity. Some authors have suggested that the administration of these drugs may also decrease BIS values and overestimate the degree of patient’s sedation. Several studies, most of them conducted in adult patients, have analysed the impact of NMB on BIS, with contradictory results. Many have found that neuromuscular blocking agents (NMBAs) decrease the EMG component of BIS, thus reducing the value of the latter. However, some authors attribute the impact of NMB on BIS to a coincidental deeper level of sedation in those cases.

Our hypothesis was that NMB does not alter the ability of BIS to monitor consciousness in sedated children in paediatric intensive care units (PICUs).

The aim of our study was to analyse the impact of the use or discontinuation of NMB on BIS values in critically ill children.

Patients and methods

We conducted a prospective observational study in a tertiary referral hospital in Madrid, Spain, between 2011 and 2012. We included all patients aged 1 month to 16 years admitted to PICU during the period under study that were monitored with BIS and required infusion of NMBAs. We excluded patients with a duration of NMB of less than 6 h and those with seizures or encephalopathy that could affect BIS values. The study was approved by the local ethics committee.
We collected data on demographic (age, sex) and clinical characteristics (reason for admission, underlying disease), haemodynamic parameters (blood pressure, heart rate, central venous pressure and urine output), inotropic therapy, mechanical ventilation and reason for using NMB. Sedatives and analgesics drugs were administered per the PICU protocol, which adheres to the guidelines of the Sociedad Española de Cuidados Intensivos Pediátricos (Spanish Society of Paediatric Intensive Care). The protocol includes the rotation of different sedative and analgesics drugs with the aim of minimising withdrawal symptoms on discontinuation of opioids and benzodiazepines. We recorded the administered sedatives and analgesics and their dosage. The NMBA used in every case was vecuronium, always given at a rate of 0.1 mg kg/h.

Bispectral index monitoring was performed with a BIS XP Aspect Medical Systems® monitor and paediatric BIS sensors. Bispectral index values were recorded continuously, as were values of electromyographic (EMG) parameters, the signal quality index (SQI), the total power (TP) and the spectral edge frequency (SEF). We measured and recorded BIS parameters, the blood pressure (BP) and the heart rate (HR) 30 min before initiation of NMB and 6, 12 and 24 h thereafter. We also measured and documented the same variables were also before discontinuing BNM, and 6, 12 and 24 h after discontinuation. At the same time, we monitored the level of pain and of sedation using internationally validated scales such as the COMFORT behaviour scale and the pain ladder, and adjusted the infusion of sedatives and analgesics based on the resulting scores.

We defined moderate sedation as a BIS value of 40–60 and deep sedation as a BIS value of less than 40.10 We discarded BIS values when the signal quality index was less than 60% or the impedance level was greater than 10 kΩ.

Statistical analysis

We analysed the data using the software SPSS Statistics version 19. We used the Fisher exact test to compare frequencies and the Mann-Whitney U test to compare quantitative variables. Also, we used the Wilcoxon test to compare BIS, EMG, SQI, BP and HR values before and after NMB. We analysed the correlation between nonparametric variables by means of the Spearman rank correlation coefficient. We defined statistical significance as a p-value of less than 0.05.

Results

The analysis included 35 patients with a mean age of 30 months (range, 2–288 months), 52.9% male. The primary diagnosis in 85% of cases was postoperative care after cardiac surgery, followed by head injury (9%) and bronchiolitis (6%). The most frequent reasons for use of NMB administration were haemodynamic instability (low cardiac output, ECMO, junctional ectopic tachycardia; 49%), improvement of patient-ventilator synchrony (23%), pulmonary hypertension (14%) and increased intracranial pressure (6%).

Fig. 1 presents the BIS, EMG and SQI values. The SQI was above 80% at all times. Before administration of NMBA, patients were under moderate-to-deep sedation (mean BIS,
46.3 ± 14.9). The mean EMG value before starting the NMB infusion was 34.9 ± 9.4.

We did not observe significant changes on BIS values with the administration of vecuronium infusion (Fig. 1). However, we found a small but significant increase in BIS values 6 h ($P = .001$) and 12 h after discontinuing the NMBA ($P = .015$).

We observed a decrease in electromyogram (EMG) values at 6 h (34.9 ± 9.4 vs 31.2 ± 7; $P = .008$) and 12 h after initiation of NMB (34.9 ± 9.4 vs 28.6 ± 4.8; $P = .006$). There was a small significant increase in BIS on discontinuation of NMB (from 42.7 ± 11 to 48.4 ± 14.5; $P = .001$), as well as 6 and 12 h after discontinuation (51.3 ± 16.6; $P = .015$). Furthermore, EMG values increased significantly after discontinuation of NMB at 6 h ($P = .08$) and 12 h ($P = .012$). We did not find any other statistically significant changes in BIS parameters.

We did not find a significant correlation between BIS and EMG values before and after NMB. We also found no significant changes in haemodynamic parameters during the infusion or after discontinuation of NMB (Fig. 2).

There were no differences in the sedatives and analgesics used during these periods or their doses, save for the dose of fentanyl, which was significantly reduced after discontinuation of NMB (at 6 h, 2.2 ± 1.6 vs 1.9 ± 1.6; $P = .011$ and at 12 h, 2.2 ± 1.6 vs 1.7 ± 1.6; $P = .01$) (Fig. 3).

Discussion

Our study shows that the administration of NMBA in children does not alter BIS significantly, so the latter is a useful method for monitoring sedation in patients under NMB.

Bruhn observed that, after administering NMB to a volunteer, electromyographic activity could distort BIS measurements, and other research groups have since confirmed these findings. However, other studies, most of them conducted in adults, have not found significant changes in those measurements.

Weber et al. compared the effect on BIS values of a dose of muscle relaxant versus placebo after anaesthetic induction in 40 children that were undergoing surgery. They found no differences between the treatment and the placebo groups.

We conducted our study in critically ill children. Rather than analysing the effect on BIS values of a single dose of NMBA, we studied the effect of continuous infusion of NMB and its discontinuation. Our results showed no relevant changes in BIS values with administration of NMB, although we did find a small but significant increase in BIS values after discontinuation of vecuronium. However, although there was a statistically significant change in BIS values, they remained within the 40-to-60 range (moderate sedation).

Previous studies that showed that BIS was affected by NMBA were mostly performed in patients under moderate sedation or in conscious volunteers. However, studies conducted in patients under deep sedation have not found significant changes in BIS values.

This could explain the discrepancies between the findings of different studies, as EMG activity probably affects BIS values in conscious patients. When NMB is used, EMG activity decreases and causes a secondary drop in BIS values. In contrast, our patients were already under moderate or deep sedation with low EMG activity before the initiation of NMB. This probably explains why the infusion of the NMBA was associated with a decrease in EMG values and NMB dis-
continuation with minor increase in EMG values, which did not have a significant effect on the BIS.

In agreement with the findings of other authors, we observed statically significant changes on BIS and EMG values 6 and 12 h after discontinuing the NMB infusion. These changes may be explained in part by muscular contraction, but they are so small that we think they do not have any clinical significance in the assessment of the level of sedation.

In addition, we found no correlation between BIS values and haemodynamic parameters (blood pressure and heart rate), which was consistent with previous studies. A possible explanation is that these parameters are influenced by many different factors, and not only the degree of sedation or relaxation of the patient.

There are several limitations to our study. The sample size was relatively small, which could reduce the statistical validity of comparisons. In addition, all of the participants were under deep sedation because, for ethical reasons, we do not use muscle relaxation in patients with mild sedation. Furthermore, our study did not measure the degree of muscle relaxation.

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