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Correlation and agreement between bispectral index and state entropy of the electroencephalogram during propofol anaesthesia

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Background. Bispectral index (BIS) and state entropy (SE) monitor hypnosis. We evaluated the correlation and the agreement between those parameters during propofol anaesthesia and laryngoscopy with and without muscle relaxation.

Methods. A total of 25 patients were anaesthetized with propofol. At steady state (SS: BIS 40–50), they randomly received rocuronium (R) or saline (S); 3 min thereafter, a 20 s laryngoscopy was performed. Correlation (regression analysis) and agreement (Bland–Altman analysis) were evaluated before induction (baseline), at loss of eyelash reflex (LER), at SS and during the first 3 min after laryngoscopy (L).

Results. The correlation coefficient *r* (95% CI), the mean difference (MD) (95% CI), and the limits of agreement [lower-upper limits of 95% CI of MD (SD 1.96)] between BIS and SE were as follows. Overall recordings: 0.87 (0.83 to 0.90), 2.5 (1.2 to 3.0), and [−19.5 to 24.6]; Baseline: 0.45 (0.06 to 0.72), 7.6 (6.0 to 9.2), and [−2.7 to 17.9]; LER: 0.74 (0.47 to 0.88), 8.3 (3.5 to 13.2), and [−22.6 to 39.3]; SS, all patients: 0.41 (0.14 to 0.63), 2.0 (−0.5 to 4.6), and [−19.0 to 23.3]; SS, Group S: 0.36 (−0.07 to 0.68), 1.9 (−2.5 to 6.3), and [−25.0 to 28.8]; SS, Group R: 0.63 (0.32 to 0.82), 0.2 (−2.0 to 2.3), and [−14.0 to 14.4]; L, all patients: 0.49 (0.32 to 0.63), 0.7 (−1.6 to 3.0), and [−25.6 to 27.1]; L, Group S: 0.41 (0.13 to 0.63), 2.3 (−2.4 to 7.1), and [−36.7 to 41.3]; L, Group R: 0.72 (0.56 to 0.83), −0.6 (−2.2 to 1.0), and [−14.3 to 13.1]. The correlation was good except for SS in Group S. The MD was significantly different from 0 for overall recordings, during baseline and LER, but not for the other conditions. The agreement was poor except for baseline, and SS and L in Group R.

Conclusions. BIS and SE are globally well correlated. In contrast, agreement is poor as differences of more than 20 units are frequently observed, except for awake and paralysed patients.

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Depth of anaesthesia monitors which are currently available assess the hypnotic component of anaesthesia. Among them, the bispectral index™ (BIS) is commonly used to guide the administration of volatile and i.v. anaesthetics.[1–3] Spectral entropy of the EEG is another variable that has been introduced into clinical practice as an index of depth of anaesthesia.[4] It conceptually reflects the degree of complexity and irregularity of the EEG signal, and includes both the response entropy (RE) and the state entropy (SE). SE is computed over the EEG dominant frequency spectrum (0.8–32 Hz) and is designed to monitor the depth of hypnosis. RE is computed over a larger frequency spectrum also covering the frontal EMG activity (0.8–47 Hz), and is designed to reflect the nociceptive–anti-nociceptive balance during general anaesthesia. As BIS and SE do perform well in monitoring one of the pharmacodynamic effects of anaesthetic agents, that is the hypnotic component of anaesthesia, the clinician could be tempted to use both techniques interchangeably. However, these techniques differ regarding their respective algorithm, scale and the delay

between EEG acquisition and screen values availability. One may therefore expect that BIS and SE do not agree in several circumstances.

Comparison of measurement techniques can rely on the calculation of their respective correlation coefficients or prediction probability values with pharmacokinetic or pharmacodynamic parameters. In that way, each technique is evaluated on its own behalf and its global performance is compared with that of others.[5 6] It is also possible to calculate the correlation coefficient between two methods. However, high correlation does not necessarily mean good agreement.[7] Agreement between two measurement techniques is best assessed by the analysis described by Bland and Altman,[7] which considers the difference between two methods against their mean.

The aim of this prospective blinded study was to assess correlation and agreement between BIS and SE during induction of anaesthesia using a propofol target-controlled infusion, during a steady-state level of hypnosis, and during nociceptive stimulation, either in the presence or in the absence of neuromuscular blocking agents.

Methods

Following approval by the Regional Hospital Ethics Committee and informed consent, 25 adult (ASA status I or II) patients undergoing routine surgery under general anaesthesia were enrolled in this prospective blinded study.

Anaesthesia and monitoring

Premedication consisted in alprazolam 0.5 mg and atropine 0.5 mg given orally 1 h before surgery. Upon arrival in the operating room, patients were equipped with a standard anaesthesia monitoring (Datex-Ohmeda™ S/5™, Helsinki, Finland). The BIS was monitored using the XP device (version 4.0) and a specific quatro sensor (Aspect Medical Systems, Newton, MA, USA and Leiden, The Netherlands). The EMG activity provided by the same monitor was also recorded (power in the frequency band 70–110 Hz, in dB). SE was monitored with the Datex-Ohmeda S/5 Entropy Module (M-Entropy™), using a specific entropy sensor (Datex-Ohmeda Division, Instrumentarium Corporation, Helsinki, Finland). The BIS sensor was appropriately applied on the left side of the forehead and the entropy sensor on the right side. Neuromuscular transmission was monitored by accelerography and assessed using the train of four (TOF) stimulation mode. In all patients, general anaesthesia was induced using a propofol target-controlled infusion (model of Marsh[8]) to achieve a BIS value between 40 and 50 defined as the steady-state (SS). Effect-site concentration of propofol was initially targeted at 2.5 $\mu g\ ml^{-1}$ and increased by steps of 0.5 $\mu g\ ml^{-1}$ after 4 min if necessary. During induction, all patients were managed by the same anaesthetist blinded to the study protocol, who continuously assessed the level of consciousness. After loss of the eyelash reflex (LER), patients were ventilated with a face mask. Once SS conditions were achieved, the target concentration of propofol was not further changed and patients randomly received either 0.6 mg kg^{-1} rocuronium (Group R; n=13), or the same volume of saline (Group S; n=12); 3 min thereafter, a 20 s laryngoscopy was applied. Randomization was performed using a computer-generated randomization list provided to the nurse in charge of preparing anaesthetic medications.

Data acquisition and analysis

BIS, SE and EMG activity were continuously recorded using the Rugloop II© monitor (Demed, Temse, Belgium). Each variable was averaged over 1 min immediately after the following nine time points: before induction (Baseline), at LER, at SS, at rocuronium or saline injection (R/S), 2 min after (R/S+2), and 0, 1, 2 and 3 min after laryngoscopy (L). One patient from group S was excluded from the study because of unreliable entropy recording.

Correlation and agreement were assessed for the following conditions of recording, including n data pairs (number of patients×number of time points of recording) in each case: overall recordings (n=24×9=216), baseline (n=24), LER (n=24), SS in the absence of rocuronium [(SS in Group R)+(SS, R/S and R/S+2 in Group S), n=13+(11×3)=46], SS after rocuronium or saline (R/S and R/S+2 in Group R or in Group S, n=13×2=26 for Group R and n=11×2=22 for Group S), and during L for all patients (n=24×4=96), for patients of Group R (n=13×4=52) and for patients of Group S (n=11×4=44). Correlation between BIS and SE was assessed using classical least square linear regressions (LSRs). A sigmoid relationship between BIS and SE was also sought using LSR after logistic transformation of SE data for the entire set of recordings (n=216). Logistic transformation consisted in calculating logit(SE)=LOG [SE/(91−SE)], where LOG=base 10 logarithm and 91=maximum possible value of SE. Agreement between the two indices was evaluated by a Bland–Altman analysis.[7] The 95% CI of the mean difference between BIS and SE served to test the null hypothesis that this difference was not significantly different from 0. The limits of agreement were defined as the lower limit of the 95% CI of the mean difference minus 1.96 SD and upper limit of the 95% CI of the mean difference plus 1.96 SD. The G-Power© software[9] served for power calculations.

Differences in EMG activity between and within Groups R and S were assessed using a two-way mixed-design ANOVA and Tuckey's HSD tests for post hoc comparisons. A P-value less than 0.05 was considered statistically significant. Normality of distribution was assessed when necessary.

Results

Patients of Groups R and S were comparable in terms of age, weight, height and gender distribution as shown in Table 1.