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Variation of bispectral index under TIVA with propofol in a paediatric population

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Background. In this prospective observational study, we aim to explore the relationship between age and bispectral index (BIS) values at different plasma concentrations of propofol.

Methods. Fifty children aged from 3 to 15 yr were included. Anaesthesia was induced using a target-controlled infusion of propofol with the Kataria pharmacokinetic model together with a bolus of remifentanil followed by a continuous infusion rate at 0.2 $\mu g\ kg^{-1}\ min^{-1}$. Target plasma propofol concentration was initially stabilized to 6 $\mu g\ ml^{-1}$ and continued for 6 min. The target was then decreased and stabilized to 4 $\mu g\ ml^{-1}$ and then to 2 $\mu g\ ml^{-1}$. BIS values, plasma propofol concentration, and EEG were continuously recorded. In order to explore the relationship between variations in propofol concentration and the EEG bispectrum, we used a multiple correspondence analysis (MCA). Results are shown in median (range).

Results. We found no statistical difference between BIS values with propofol 6 $\mu g\ ml^{-1}$ [23 (12–40)] and 4 $\mu g\ ml^{-1}$ [28 (9–67)]. At 2 $\mu g\ ml^{-1}$, BIS was significantly different [52 (24–71)], but a significant correlation between the age of children and BIS values was found (r^2=0.66; $P<0.01$). There was little change in children's position between 6 and 4 $\mu g\ ml^{-1}$ in the structure model of the MCA. From 4 to 2 $\mu g\ ml^{-1}$, the position of children moved only on axis 2.

Conclusions. These results showed the difficulty to interpret BIS values because of the absence of significant change for higher plasma propofol concentration variation or because of the link with age for the lower plasma concentration.

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In the paediatric population, the ability of the bispectral index (BIS) to accurately follow variations in anaesthetic agent concentration and evaluate depth of anaesthesia remains controversial. It has been shown in recent studies using various volatile anaesthetic agents that BIS values were linked to the age of children irrespective of the volatile agent used.[1–5] In addition, there is good evidence that BIS values are agent-dependent for the same level of minimal alveolar concentration (MAC).[4 6 7]

Propofol is widely used for both sedation and general anaesthesia in adults and children. Few studies have attempted to evaluate BIS variation under target-controlled infusion (TCI) with propofol in a paediatric population.

In this prospective observational study, we aim to explore the relationship between age and BIS values at different estimated plasma concentrations of propofol and to analyse the EEG bispectrum modifications induced by this hypnotic.

Methods

After approval from the Humans Studies Committee, and with written parental consent, 50 ASA I or II children aged from 3 to 15 yr were included into our study. Children with central neurological disease and those taking medication acting on the central nervous system

were excluded. No children were premedicated. Before arriving in the operating department, an EMLA patch was applied on both hands. Before induction of anaesthesia, BIS paediatrics leads (Aspect Medical Systems, Newton, IL, USA) were placed according to the manufacturers instructions and connected to Aspect XP™ device. EEG leads (3M Red Dot Silver/Silver Chloride model 2269T, 3M Health Care, St Paul, USA) were placed adjacent to the BIS leads.

After i.v. access had been obtained, the children were pre-oxygenated. Thereafter, anaesthesia was induced with a bolus of remifentanil (1 μg kg^{-1} more than 1 min) followed by a TCI of propofol using an Asena® PK syringe pump (Alaris® Medical Systems, Alaris Medical UK Ltd, Basingstoke, UK) incorporating the Kataria pharmacokinetic (PK) model (weight-proportional age-adjusted).[8] Remifentanil was continued at 0.2 μg kg^{-1} min^{-1} until the end of the study protocol. The initial target plasma propofol concentration was set at 7 μg ml^{-1} to permit intubation without the use of neuromuscular blocking agents. After tracheal intubation all children were ventilated in oxygen/air to maintain normocapnoea. Target plasma propofol concentration was then decreased to 6 μg ml^{-1} and after this target was reached, it was maintained for 6 min to obtain a stationary EEG bispectrum (defined as the absence of statistical difference in bispectral parameters during the last minute of each steady state). The target plasma concentration was then decreased to 4 μg ml^{-1} and maintained at this level for a further 6 min, and then finally the target plasma concentration was decreased to 2 μg ml^{-1} and maintained for the final 6 min of the study protocol. During the study period, there was no surgical stimulation. No other drugs were administered. BIS values and plasma concentration of propofol were continuously recorded using the Rugloop II ® device (Demed, Temse, Belgium). Raw EEG was recorded using PowerLab™ software (AD Instruments, Castle Hill, NSW, Australia). All data were recorded throughout the case. Raw EEG and EEG bispectrum were mathematically processed as described previously.[1] EEG bispectrum was estimated on successive epochs of 20 s using MATLAB© software. Each EEG bispectrum was divided into 36 blocks of frequency of coupling (Fig. 1). The mean of the bispectrum for each block was then calculated so that each child was represented by 36 descriptors evolving over the time of recording.

For statistical analysis, correlation between BIS values (taken as the median value during the last 30 s of each plateau phase) and age of children was evaluated by means of a Spearman test. A Wilcoxon test was used to establish significant changes in parameters at various points during the decrease of propofol plasma concentration. In order to explore the relationship between variations in plasma propofol concentrations and the EEG bispectrum, we used a multiple correspondence analysis (MCA). The structured model of the MCA was derived from previous recordings of children anaesthetized with sevoflurane, and was explained in detail in this study.[1] The change in position of children within the structured model of the MCA is determined only by changes in the EEG bispectrum during the decrease of plasma propofol concentration. All results are described as median (range). A P-value of <0.05 was considered significant. All statistical analyses were performed with the BI©LOGINSERM 1979–87 software.

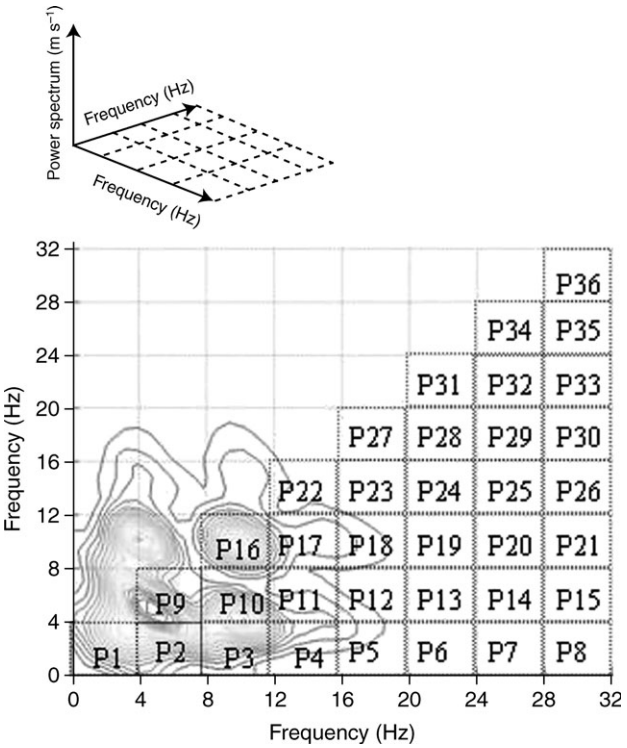

Fig 1 An example of the representation of the 36 frequencies of coupling (Pi) of the bispectrum calculated every 20 s for one child's EEG (MatBis).

Results

Complete recordings were obtained in all 50 children. The median (range) age and weight was 95 months (40–182) and 25 kg (13–60), respectively. Physiological variables at the various target plasma propofol concentrations are shown in Table 1. The BIS values at different plasma propofol concentrations are represented in Figure 2. We found no statistical difference between BIS values under anaesthesia with propofol 6 μg ml^{-1} 23 (12–40) and

Table 1 Physiological variables at different plasma propofol concentrations. SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; HR, heart rate

	Awake	6 μg ml^{-1}	4 μg ml^{-1}	2 μg ml^{-1}
SBP (mm Hg)	114 (87–147)	91 (121–76)	90 (73–112)	8 (70–105)
DBP (mm Hg)	60 (42–89)	47 (39–76)	46 (30–70)	43 (25–62)
MAP (mm Hg)	72 (55–94)	57 (50–86)	56 (44–79)	55 (38–77)
HR (beats min^{-1})	82 (45–115)	81 (40–104)	75 (49–99)	72 (59–86)