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Ephedrine, phenylephrine and BIS during propofol anaesthesia

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EDITOR:

We congratulate Takizawa and colleagues [1] on their interesting study examining the effect of commonly used vasopressors on bispectral index scores (BIS) during propofol anaesthesia supplemented with high-dose fentanyl. This has complemented the earlier work of Ishiyama and colleagues [2] who performed a similar study with sevoflurane. Both these studies have demonstrated a statistically significant increase in BIS following ephedrine administration for intraoperative hypotension, which is an everyday occurrence, particularly following induction of anaesthesia. Therefore, the question posed by Takizawa is important. What is not clear, however, is whether this apparent 'lightening' of anaesthesia with ephedrine is clinically significant or not. Clearly, with a reported incidence of awareness of 0.07–0.18% [3], a much larger cohort of patients would be required to demonstrate clinically significant changes in the incidence of awareness. However, we have some concerns regarding the methodology of the reported study.

The effect of opioids on BIS is less well characterized compared with volatile and intravenous anaesthetic agents. Barr and colleagues [4] found that patients given fentanyl $10 \mu\text{g kg}^{-1}$ supplemented with 0.5 mg kg^{-1} propofol at induction, lost consciousness at a much higher BIS (median 91; range 78–98), compared with patients given fentanyl alone (median 80; range 45–94). The 'deeper' plane of anaesthesia was maintained for 10 min after induc-

tion. In the current study, clinicians were free to give fentanyl $10\text{--}20 \mu\text{g kg}^{-1}$ at induction. Although this is a routine practice for cardiac patients, data on fentanyl dosage between groups would have perhaps added weight to the finding that BIS scores were higher in the ephedrine group. In this way, any pharmacological interaction between propofol and fentanyl could be accounted for.

Eight patients (40%) in the ephedrine group had BIS scores greater than 60, 10 min after the ephedrine was given. The inference is that these patients were at risk of awareness. There is no report by the authors of postoperative interviews with these patients to check for any recall, either implicit or explicit. Therefore, although the authors' conclusions are just and BIS has been shown to reduce the incidence of awareness in high-risk patients [5] (e.g. off-pump coronary artery bypass), the clinical ramifications of this study remain unclear. Indeed, it would seem counterintuitive to administer ephedrine for hypotension and then to have to deepen the anaesthetic for fear that the patient became aware.

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Reply

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EDITOR:

We thank Dr McCahon and colleagues for their interest in our study [1]. Dr McCahon enquires whether the effect of ephedrine on bispectral index scores (BIS) values were clinically significant or not. In this study, we examined whether ephedrine increased BIS values during propofol anaesthesia as it does during sevoflurane anaesthesia [2] and whether ephedrine decreased propofol concentrations.

Johnson and colleagues [3] reported arousal following isoprenaline administration during propofol anaesthesia. They also examined the effect of intravenous epinephrine on BIS and sedation, reporting that mean BIS values increased from 63 to 76 and exogenous catecholamines seemed to display an arousal effect [4]. This could be due to changes in neurotransmitter levels in the brain. The adrenergic system has a role to play in the process of arousal from anaesthesia, and this has been previously demonstrated [5]. β -receptors in the reticular-activating system interact with the information processing in the thalamus. However, another possible explanation that propofol concentration decreased due to increased cardiac output on administration of a catecholamine had not been examined. In our previous study, we showed decreases in propofol concentration with increased cardiac output following dopamine administration [6].

Ephedrine exerts a potent stimulating effect on the central nervous system [7]. Ishiyama and colleagues [2] reported that ephedrine increased BIS during sevoflurane anaesthesia. We examined the effect of ephedrine on propofol concentrations and on BIS. Our study showed that ephedrine increased BIS to >60 in eight of 20 patients without changing the propofol concentrations. In our study, post-operative interviews revealed that there were

no patients who had any recall during the surgical procedure. No other study reports arousal following ephedrine administration. As suggested by McCahon and colleagues, the clinical significance in the effect of ephedrine on BIS is not clear from our study. Further work on anaesthetic depth is required concerning the clinical significance of the effect of drugs that act on the central nervous system.

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