CORRESPONDENCE

PHARMACOKINETICS OF PROPOFOL

Sir,—We read with interest the pharmacokinetic study of a propofol infusion during cardiac surgery by Massey and colleagues [1]. It is illogical to infuse propofol after induction of anaesthesia at a constant rate of 4 mg kg\(^{-1}\) h\(^{-1}\) during which the desired blood concentration of greater than 1 \(\mu\)g ml\(^{-1}\) is not achieved until approximately 10–15 min. While it is debatable that 1 \(\mu\)g ml\(^{-1}\) is sufficient to produce anaesthesia, we believe that it is not acceptable to achieve this as late as 10 min after induction and intubation.

It would seem more appropriate either to give an initial bolus dose and start the propofol infusion simultaneously, or to start the constant infusion before induction. Although an induction dose of propofol 2.5 mg kg\(^{-1}\) is associated with hypotension [2], a reduced dose, given slowly, is less likely to cause haemodynamic instability [3].

Using a computer model [4] we have calculated that the bolus dose should be 0.4 mg kg\(^{-1}\), with an infusion of 4 mg kg\(^{-1}\) h\(^{-1}\). The rapidity with which a calculated blood concentration of propofol exceeds 1 \(\mu\)g ml\(^{-1}\) is shown in figure 1. Also demonstrated is the considerable delay, using Massey’s regimen, in achieving the concentration of propofol required to guarantee hypnosis.

In addition, the dose of midazolam used at induction (0.03 mg kg\(^{-1}\)) does seem inappropriately small (a maximum of 3 mg in a patient of 127 kg) and, although there were no reports of awareness on direct questioning, with the small number of patients in their study, this may reflect a lack of recall rather than awareness per se.

We feel that, with the procedure as described, patients are at risk of awareness during the first 15 min, especially with a technique that did not involve nitrous oxide. A recent editorial [5] has cautioned us to be prudent with new methods of anaesthesia, and one such as this may bring the technique of i.v. anaesthesia rapidly into disrepute.

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REFERENCES


Sir,—Thank you for giving us the opportunity to respond to the comments in this letter.

It is not only debatable, but is unlikely that a blood concentration of propofol 1 \(\mu\)g ml\(^{-1}\) alone provides anaesthesia, especially for patients undergoing open heart surgery. In this context, we were using propofol as a hypnotic. We consider that our use of propofol following induction of hypnosis is not illogical, but is analogous to the use of gaseous agents following i.v. induction agents.

In our anaesthetic regimen, analgesia was provided by premedication including papaveretum i.m. (20 mg in seven patients, 15 mg in three patients) according to sex and weight and alfentanil i.v. to a total dose of 100 \(\mu\)g kg\(^{-1}\) plus 60 \(\mu\)g kg\(^{-1}\) h\(^{-1}\).

Hypnosis was induced by the sedative effects of premedication and midazolam i.v. according to patient response (3 mg in eight patients, 2.5 mg in two patients). Ninety seconds after midazolam, all patients were unresponsive to command and to manual inflation of the lungs using a mask circuit. Hypnosis was then maintained using the propofol infusion.

The discussion of Dr Sidhu and colleagues relates to whether i.v. propofol 0.4 mg kg\(^{-1}\) (approx. 30 mg) followed by an infusion of 4 mg kg\(^{-1}\) h\(^{-1}\) provides more reliable hypnosis than a hypnotic dose of midazolam i.v. followed by an infusion of propofol 4 mg kg\(^{-1}\) h\(^{-1}\) in the presence of full opioid analgesia. This cannot be answered by either measuring or computing drug concentrations in the blood, as the sedative effects of the opioids and hypnotics used are cumulative.

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REFERENCES