The potential use of intralipid to minimize propofol's cardiovascular effects

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To the Editor

Many reports exist which advocate the use of intralipid to reverse local anesthetic cardiovascular toxicity. The precise mechanism of action, while unknown at the present time, may include a combination of reduced tissue binding of local anesthetic by a plasma-lipid phase and a beneficial metabolic effect involving cardiac mitochondria.¹ We hypothesized that intralipid can also function as a cardiovascular reversal agent for propofol.

Despite suggestions that physostigmine² or aminophylline 3 can reverse the sedative-hypnotic effects of propofol, no medication currently exists which can directly reverse the cardiovascular effects of propofol. It remains a matter of supportive management while allowing the effects of propofol to dissipate. From a recent study involving aging of resistance systemic arteries *ex vivo*, we found that vascular relaxation was induced by propofol concentrations between 1 and 100 μM (unpublished results). In a similar experiment, we also found that propofol-induced relaxation [100 μM (0.02 mg ml⁻¹ final concentration); Novopharm, ON, Canada] was antagonized by the administration of intralipid 20% at a final concentration of 2–4% soybean oil (Baxter, ON, Canada). Our method of isolating arteries has been described previously.⁴ Briefly, rat mesenteric arteries 100–200 μm in diameter were excised and subjected to isometric tension studies utilizing a wire myograph system. These arteries were pre-constricted with phenylephrine (PE) and were relaxed by propofol. After the addition of

propofol (0.02 mg ml⁻¹ final concentration), intralipid 20% (500–1,000 μl in 5 ml tissue bath) consistently reversed the relaxation caused by propofol in four out of four samples. In contrast, the addition of an equivalent volume of saline (control) did not reverse the propofol-induced relaxation (Fig. 1). Based on these preliminary findings, we extrapolated that approximately 50–100 ml of intralipid 20% may be required to reverse the effects of 1 ml of commercially available propofol (10 mg ml⁻¹). Additionally, intralipid itself did not induce constriction in the absence of PE and was not toxic to the arteries, since they exhibited PE constriction following intralipid washout.

Propofol is available commercially as a mixture in intralipid, where soybean oil holds the bulk of the propofol.⁵ Therefore, we propose that intralipid can serve as a “propofol mop” by extracting propofol from its site of action (e.g., hydrophobic pockets of membrane proteins). It is unlikely to be a dilutional effect, since the corresponding volume of saline added to the tissue baths did not reverse the vasodilation. We suggest that intralipid may inhibit the untoward effects of propofol at the vascular level, since previous findings have demonstrated that only small amounts of intralipid cross the blood-brain barrier.⁶ Therefore, with the administration of intralipid, the actions of propofol on sedation/consciousness have the potential to be unaltered, without cardiovascular depression. As mentioned above, intralipid is being advocated as an antidote for local anesthetic toxicity, and we propose an additional role to minimize propofol's untoward cardiovascular side-effects. Similar to treatment for local anesthetic toxicity, further studies taking the bench-to-bedside approach will need to be completed to determine the minimum amount of intralipid necessary to reverse the cardiovascular effects of propofol *in vivo*. Dose-finding studies utilizing this type of

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Fig. 1 Intralipid, but not an equivalent volume of saline, reverses propofol-induced vasodilation. Representative traces for the effects of (a) intralipid vs (b) saline control, and (c) mean data demonstrating reversal of propofol-induced relaxation in resistance mesenteric arteries by the addition of intralipid ($n = 4$ per group); $*P < 0.05$ intralipid vs control

experimental set-up, followed by the use of whole animal models, will be required to address this question.

Conflicts of interest None declared.

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