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Incompatibility of Propofol Emulsion with Anesthetic Drugs

To the Editor:—We were recently performing a propofol-containing anesthetic in a patient undergoing cardiac surgery. After cardiopulmonary bypass, we injected protamine (Protamine sulfate, Fujasawa Canada Inc., Markham, Ontario) in the same intravenous line as our propofol infusion (Diprivan, Zeneca Pharma, Wilmington, DE), and large globules were formed. This observation was reproduced in test tubes where an equal volume of undiluted propofol and protamine were mixed. A separation of the oil and aqueous phases of propofol was noticed immediately, even when a small quantity of protamine was added to the emulsion. Because propofol emulsion is similar to Intralipid 10% and Travamulsion 10%, we repeated the same process, mixing protamine and Travamulsion 10%. The same "cracking" of the emulsion was observed, suggesting that the emulsion, rather than propofol *per se*, is responsible for the incompatibility.

The clinical significance of this physical incompatibility is uncertain. Fat emulsions for intravenous use are manufactured with a particle diameter of 0.2–0.4 μm . Particles larger than 6 μm in diameter, as might occur with emulsion instability, have a potential for embolization, specially in the lungs.¹ Thus, fat emboli might be a problem but an unlikely one because the amount of separated fat particles that would be infused after a single dose of protamine would be small.

Physical incompatibility may also result in altered drug potency. Using high-performance liquid chromatography, Bhatt-Mehta *et al.* showed that only 72% of the initial propofol concentration remained after 5 h when propofol and 1.5% amino acid parenteral nutrition solution were combined.² Therefore, a chemical incompatibility can result in the infusion of a lower concentration of the drug than intended. However, we do not know if the decreased potency of propofol would be significant in the context described.

As propofol is opaque, it is often difficult to determine incompatibilities visually. Micheals *et al.* investigated two new methods of evaluating compatibility with propofol, mainly by adding methylene

blue to the mixtures or by separating the aqueous phase of propofol to improve visualization of physical incompatibilities.³ The authors reported that 69 of 77 drugs tested, several of which are used commonly by anesthesiologists, showed immediate evidence of physical incompatibility.³ Our observation suggests that protamine be added to the (long) list of drugs known to be incompatible with propofol. Further, we recommend that propofol be administered in a dedicated intravenous line.

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