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LETTER TO THE EDITOR

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# A well-known but rarely seen interaction: propofol with lignocaine

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To the Editor,

Propofol is considered an excellent intravenous anesthetic agent. However, a 30–70% incidence of pain associated with its injection is a significant source of patient discontent. Injection pain and discomfort rank as the sixth most crucial perioperative issue (Desousa 2016). Several techniques have been employed to reduce injection discomfort, including the use of the forearm and antecubital veins, freezing or warming the injectate, and aspirating blood before injection. Pre-treatment or contemporaneous administration of thiopentone, pethidine, fentanyl, dexamethasone, nitroglycerine, ketorolac, and local anesthetics has also been considered. However, the most common strategy includes the administration of lidocaine injection immediately prior to propofol injection or combining propofol and lignocaine in the same syringe (Overbaugh et al. 2002).

At our institute, we blend 20mg of 2% lignocaine with 9 ml of 1% propofol (Fresofol® 1% MCT/LCT) to alleviate injection discomfort. We prepared the same for a case of trans-sphenoidal surgical excision of a pituitary tumor utilizing conventional aseptic measures. After 90 min of drug preparation, we saw propofol precipitating as a distinct layer in the syringe, as indicated (Fig. 1). The expiry dates on the vials were verified and confirmed, the contents were destroyed, and a new combination was made using a different batch of medicines. The manufacturer advises shaking the vial before use and using it soon after aspiration. Nevertheless, preparing the combination before taking up the cases is customary.

Propofol is an alkylphenol (2,6 di-isopropyl phenol), insoluble in water, and lipid soluble. It is oil at room temperature. The current MCT/LCT propofol preparation includes 10% soybean oil, 2.5% glycerol, and 1.25% pure egg phosphatide with 0.008% disodium edetate (EDTA) as a bacterial growth suppressor. It is a milky, viscous substance with a pH of 7 and a pKa of 11 (Overbaugh et al. 2002).

In referenced case, the addition of 2% lidocaine (20mg) to 1% propofol (10ml) caused macroscopic precipitation at 90 min due to the instability of the emulsion when the case was delayed for 90 min after its preparation. On the other hand, propofol-lignocaine combination turns yellow in color after approximately 6 h of exposure to air due to the oxidization of propofol to quinone. The presence of sodium metabisulfite as a bacteriostatic agent speeds up the process of oxidation to quinone but EDTA propofol emulsion stayed white at all times. Hence, precipitation and oxidation are two distinct concepts associated with propofol-lignocaine combination (Baker et al. 2003, Damitz et al. 2016).

Masaki et al. examined different mixtures of lignocaine and propofol under scanning electron microscopy. They first detected droplets with diameters of 5 μm at 30 min; however, macroscopic evidence was seen at 3 h. They further observed a maximal increase of droplet diameter up to 20μm at 24 h after the addition of 40-mg lignocaine. Thus, they concluded that mixing more than 20 mg of lignocaine with 20 ml of propofol should be avoided or used immediately. They also emphasized that long-term infusions of such mixtures should not be used, as in intensive care settings, and a new mixture should be made whenever

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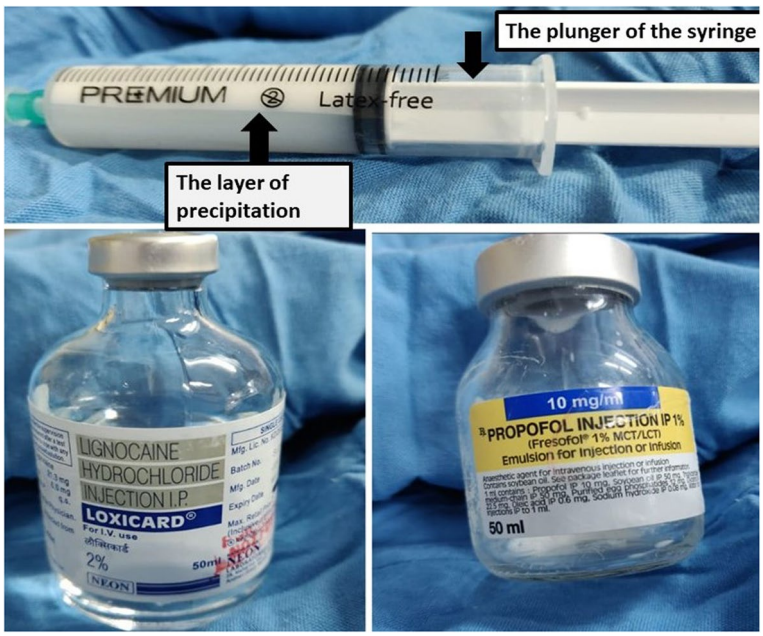


**Fig. 1** Distinct layer of precipitation of propofol-lignocaine in a syringe

necessary. Furthermore, a droplet diameter of 5μm or more should not be allowed in intravenous infusions as it poses a risk of fat embolism (Masaki et al. 2003).

Lilley et al. investigated the macroscopic and microscopic stability of mixtures of propofol and lignocaine ranging from 200:10 to 200:50 mg and reported that an oily surface layer appeared 75 min after the addition of 40-mg lignocaine to 200-mg propofol. They discovered that adding even 20-mg lignocaine to 90-mg propofol caused a dose and time-dependent separation of propofol as an oily layer and a reduction in its concentration in the mixture, which was clinically significant with higher doses of lignocaine (Lilley et al. 1996).

Park et al. reported that globule size had increased considerably at 6 h (to 51.76 ± 0.62 micro m) when 30 mg of lignocaine was added (Park et al. 2003).

In conclusion, clinical practice should consider the emulsion instability caused by adding lignocaine to propofol, particularly when a larger dose of lignocaine is added or when there is a delay between preparation and administration.

#### Abbreviations

| | |
|---|---|
| MCT | Medium chain triglyceride |
| LCT | Long-chain triglyceride |
| pH | Potential of hydrogen |
| pKa | Acid dissociation constant |
| μm | Micron or micrometer |

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## Declarations

#### Ethics approval and consent to participate
Letter to editor does not require ethical committee approval and a registration number. This report was purely an observation of the prepared drug. It does not contain any patient-related information and neither has it caused any harm to a patient.

#### Consent for publication
Not applicable.

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