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THE POISON PEN

Comment on Complications Following Antidotal Use of Intravenous Lipid Emulsion Therapy (Levine et al., J Med Toxicol 2013)

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A published case series of Levine et al. reporting complications following antidotal use of intravenous lipid emulsion (ILE) is a well-written and much needed critical analysis [1]. In addition to the clinical complications of acute pancreatitis and respiratory distress syndrome, the authors also address the analytical complications of lipemic interference. ILE interferences can lead to delayed reporting of time-sensitive results with dire consequences as demonstrated by the loss of a potential organ donor candidate. Additionally, erroneous results may be used to guide therapy [2].

In two of the six cases, chemistry results were delayed for over 16 h despite ultracentrifugation. We find this intriguing as it contradicts our in vitro study which demonstrated that re-centrifugation of lipemic samples (prepared by the addition of Intralipid 20 % to serum) reduced lipemia to levels at which laboratory studies could be performed. To assist the readership faced with similar clinical scenarios, it would have been useful if the authors had reported which chemistries and analytical methods were affected and the methodology used to separate the lipid layer from the serum.

The CLSI (Clinical and Laboratory Standards Institute) interference testing guidelines recommend ultracentrifugation to clear lipemic samples with triglycerides of up to 3,000 mg/dL (33 mmol/L) [3]. Lipid clearance by ultracentrifugation requires the generation of 200,000–600,000×*g*, forces not achievable by the centrifuges found in most hospital laboratories.

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However, brief high-speed centrifugation (10,000–14,000×*g* for 10–15 min) of serum or plasma with either exogenously supplemented triglycerides (e.g. ILE) of up to 77 mmol/L (6,900 mg/dL) or endogenous elevated triglycerides of up to 43 mmol/L (3,900 mg/dL) removes enough lipid to permit laboratory analyses [2, 4]. Bench-top micro-centrifuges capable of generating the required forces are typically available in hospital laboratories.

The following clarifications may facilitate appropriate application of these "clean up" methodologies and avoid potential difficulties:

1. ILE solutions contain glycerol in order to maintain a physiologic osmolality [5]. Most clinical methods will overestimate triglyceride concentrations in ILE supplemented samples or treated individuals due to glycerol interference [6]. Depending on the time since treatment and the amount of ILE added, reported triglyceride concentrations may be over 200 % actual levels [4]. While this interference will not be removed by centrifugation, it can be compensated for by glycerol blanking.
2. Due to its lower density, lipid will float on top of serum once separated. This may make analysis of the underlying serum difficult. In order to avoid recontamination, the lipid-cleared infranatant can be carefully transferred into a clean tube using glass pipettes to slowly aspirate approximately 2/3 of the serum, avoiding any remixing. In the presence of extremely high triglyceride concentrations or difficult separations, centrifugation can be repeated as long as enough serum has been collected.

The group of Levine voices a necessary critique of the increasingly liberal use of a potentially beneficial treatment that itself can have adverse effects. The inclusion of peak glycerol-

blanked triglyceride concentrations as well as affected and unaffected laboratory analyses (including methodologies, timing and concentrations) in future studies will help to refine appropriate use of resuscitative ILE therapy.

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