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Lipid emulsion resuscitation for intractable calcium channel blocker toxicity in pediatric patients

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To the Editor:

I read with interest the report entitled, "Effect of intravenous lipid therapy in critically ill pediatric patients with calcium channel blocker toxicity," recently published in The Turkish Journal of Pediatrics.[1] Previous studies have shown lipid emulsion, initially designed for intravenous nutrition, in treating cardiovascular collapse due to toxic levels of non-local anesthetics in pediatric patients.[2,3] I would like to comment on the fundamental mechanism and recommend a dosing regimen for lipid emulsion. First, the underlying mechanism of lipid emulsion resuscitation involves both direct and indirect effects.[2] The widely accepted theory behind this resuscitation method is the lipid shuttle mechanism.[2] According to this theory, the lipid component of the lipid emulsion absorbs highly lipid-soluble drugs (with a log P [octanol to water partition coefficient] value exceeding 2, such as bupivacaine, verapamil, and amlodipine with log P values of 3.41, 3.79, and 3, respectively) from the heart and brain.[2] Subsequently, the lipid emulsion containing the lipid-soluble drugs is transported to the liver, muscle, and adipose tissue for detoxification and storage.[2] The direct effects of lipid emulsion resuscitation encompass a range of actions such as positive inotropic effects, supplying fatty acids, inhibiting mitochondrial dysfunction, restraining nitric oxide release, and promoting glycogen synthase kinase-3β phosphorylation.[2] In light of previous findings, the increase in ejection fraction and blood pressure following the administration of lipid emulsion in this study could be linked to two factors: first, the removal of highly lipid-soluble calcium channel blockers like verapamil and amlodipine from the heart, and, second, the positive inotropic effect mediated by the lipid emulsion itself.[2-4] Second, the lipid emulsion dosing regimen described by Yavuz et al. is as follows: "A recommended dosing regimen for lipid emulsion is an infusion of 20% solution, 1 mL/kg over 1 minute, repeated every 3 to 5 minutes for a maximum of 3 mL/kg followed by 0.25 mL/kg/min."[1,5] This dosing regimen was proposed in 2004, predating the recommended lipid emulsion regimen for local anesthetic systemic toxicity by the American Society of Regional Anesthesia and Pain Medicine:[5,6] An initial intravenous bolus of 1.5 mL/kg of 20% lipid emulsion, followed by a continuous infusion at a rate of 0.25 mL/kg/min of 20% lipid emulsion.[6] However, local anesthetic systemic toxicity primarily occurs as a result of intravascular injection of local anesthetic agents, whereas toxicity from non-local anesthetics such as calcium channel blockers typically stems from oral administration of these drugs. Consequently, the pharmacokinetics of toxicity is different. In addition, there is no established lipid emulsion dosing regimen specifically for managing non-local anesthetic drug toxicity. A 1% plasma triglyceride concentration triggers both a positive inotropic effect and scavenging of lipid-soluble drugs.[4,7] On the basis of previous findings, a suggested dosing regimen for lipid emulsion to achieve 1% plasma triglyceride levels for managing drug toxicity due to non-local anesthetic drugs is as follows: Initially administer 1.5 mL/kg of 20% lipid emulsion

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over 1 min, followed by 0.25 mL/kg/min over 3 min, and then maintain a continuous infusion of 0.025 mL/kg/min of 20% lipid emulsion.[4,7-9]

Author contribution

Study conception and design: JTS; draft manuscript preparation: JTS. The author reviewed the results and approved the final version of the article.

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Conflict of interest

The author declares that there is no conflict of interest.

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