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LETTER TO THE EDITOR

Calcium dosage in the lipid emulsion used to treat verapamil toxicity

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Dear Editor:

We have read the interesting report titled "Effect of intralipid administration on calcium therapy in verapamil toxicity," recently published in *Bratislava Medical Journal* (1). Lipid emulsions can effectively attenuate severe vasodilation induced by toxic doses of the highly lipid soluble calcium channel blocker, verapamil (2). The following comments should be considered when assessing this report. First, calcium group received 0.2 mmol kg^{-1} calcium in 12.4 mL kg^{-1} of 0.9 % normal saline delivered over 10 min. The 0.2 mmol kg^{-1} calcium dose used in this experiment corresponds to 0.008 mg ml^{-1} kg^{-1} calcium (1). As calcium was dissolved in 12.4 mL of normal saline (0.9 %) kg^{-1}, total calcium dosage is 0.0992 mg kg^{-1}. A previous study used 15 mg kg^{-1} calcium chloride (equivalent to approximately 5.45 mg kg^{-1} calcium) in a lipid emulsion treatment for verapamil toxicity (3). Thus, the calcium dosage used in this study is approximately 55-folds lower than that in the previous study (1, 3). Second, it is unclear what type of solution (intralipid or normal saline) was used to dissolve calcium (0.2 mmol kg^{-1}) in the group administered with loading dose intralipid followed by calcium (Group L-Ca) (1). Third, after the Kruskal–Wallis test was performed to analyze the data in this study, Dunn's multiple comparison tests would have been more reasonable than the Mann–Whitney test as a post-hoc test to detect a difference between groups to reduce type 1 error (4). Fourth, both the baseline and 50 % reduction in baseline heart rates were higher in the group concomitantly administered with intralipid and calcium (Group L+Ca), compared to the control or Group L-Ca (1). Thus, a mixed linear model was used to analyze heart rate among the four groups; however, comparing the percent change in heart rate from baseline following verapamil administration is more reasonable than directly comparing heart rates (1). Fifth, the lipid sink phenomenon has been widely accepted as the mechanism underlying lipid emulsion resuscitation, rendering this treatment a non-specific antidote (5). However, lipid shuttling, in which the lipid emulsion absorbs the toxic dose of highly lipid soluble drugs such as bupivacaine, reducing its levels in the heart, whereupon the lipid emulsion containing the lipid soluble drug is transported through the blood stream to the liver and muscle for detoxification and storage, respectively, leading to enhanced redistribution, has recently become widely accepted as the underlying mechanism (5). Although the calcium dosage used in this study is miniscule, we believe that this report contributes toward proving the efficacy of lipid emulsion treatment with either concomitant or subsequent administration of calcium for treating toxicity induced by intravenous administration of a toxic dose of verapamil.

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