Hemodynamic effects of lipid emulsion after local anesthetic intoxication may be due to a direct effect of fatty acids on myocardial voltage-dependent calcium channels

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To the Editor,

We read with great interest the review article by Dillane *et al.* on local anesthetic systemic toxicity.¹ The authors considered two hypotheses regarding the mechanism of action of lipid emulsions. The first hypothesis was pharmacological, wherein a circulating lipid sink extracts lipophilic local anesthetic from either plasma or tissues. The second hypothesis was metabolic, invoking reversion of the local anesthetic inhibition of the myocardial fatty acid oxidation. We suggest that a third mechanism could be involved, i.e., a direct stimulation of the voltage-gated calcium channels (Ca_v) of cardiomyocytes by long-chain fatty acids.² Huang *et al.* showed that long-chain fatty acids could activate myocardial Ca_v directly and then induce a dose-dependent increase of calcium current. Intralipid® solution contains mainly oleic and linoleic acids (23.5% and 53%, respectively, according to laboratory data) that induce a strong and early increase (within two minutes) of the calcium current in the cardiomyocytes.² In an isolated rat heart model perfused with L-bupivacaine solution, Stehr *et al.* observed a rapid increase in myocardial contractility and left ventricular systolic pressure after administration of a lipid emulsion.³ They attributed this response primarily to a direct inotropic effect, even though a local anesthetic

plasma-binding effect of lipids could not be excluded. Direct activation of the Ca_v by fatty acids could at last partly explain the early effects of lipid emulsions on myocardial toxicity of local anesthetics, as has been proposed for calcium channel blocking agents.^{4,5}

Competing interests None declared.

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Editor's Note: The authors of the review article: Can J Anesth 2010; 57: 368-80, respectfully declined an invitation to submit a reply to the above Letter to the Editor.

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