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Intralipid – the New Magic Bullet in Cardioprotection?

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To the Editor:

In two recent publications in *Anesthesiology*, Dr. Eghbali's group reports the attenuation of myocardial reperfusion injury (RI) in rodents by intralipid administered on reperfusion.[1,2] Taken together with another study by the same group in which intralipid prevents and even rescues pulmonary hypertension,[3] and the serendipitous landmark discoveries of lipid rescue therapy against bupivacaine-induced cardiotoxicity first in dogs[4] and then humans,[5] intralipid appears to have become a new magic bullet for cardioprotection. Nevertheless, many questions remain. Li et al.[2] state that intralipid acts through the phosphorylation of Akt/ERK1/glycogen synthase kinase-3β and ultimately leads to delayed opening of the mitochondrial permeability transition pore (mPTP). In contrast to the mPTP pore inhibitor cyclosporine-A or other proven postconditioning agents,[6,7] however, intralipid is a mixture of various different compounds: fractionated soybean oil, fractionated egg phospholipids and glycerol.[8,9] Which of these compounds is ultimately responsible for the cardioprotective effect? Is this truly a receptor mediated effect or could it simply be a metabolic switch from glucose to fatty acid metabolism that paradoxically protects the heart as suggested in another of Dr. Eghbali's publications[10] and by us?[11,12] Since intralipid is metabolized *in vivo* and its contents may reach the heart in a very different form[8] than in the isolated heart preparation, both models are difficult to compare directly in this context. Lastly, as much as delayed mPTP opening appears to be a common end-effector in many different animal models of protection against myocardial RI[13] Li et al.[2] show once more that inhibition of the mPTP may be necessary but by far not sufficient for cardioprotection: although not formally done in their study, the extent of delayed mPTP opening in control, cyclosporine-A and intralipid treated animals does not correlate with the observed degree of functional and tissue protection in the three groups. Therefore, despite these interesting findings, it may still be a long way to a potential clinical usage of intralipid in preventing myocardial RI.

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