Lipid emulsions used in parenteral nutrition induce endothelial dysfunction in porcine coronary artery rings: role of oxidative stress and cyclooxygenase-derived vasoconstrictors

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Lipid emulsions are used to provide a source of calories and essential fatty acids for patients requiring parenteral nutrition. They have been associated with hypertriglyceridemia, hypercholesterolemia and metabolic stress, which may promote the development of endothelial dysfunction. The aim of the present study was to determine the possibility that five different commercial lipid emulsions affect the endothelial function of coronary arteries, and, if so, to investigate the underlying mechanism.

Porcine coronary arteries were incubated with lipid emulsions for 30 minutes before the determination of vascular reactivity in organ chambers and the level of oxidative stress using the redox-sensitive fluorescent dye dihydroethidium (DHE). Incubation of coronary artery rings with either Lipidem®, Medlipid® or Smoflipid® (medium-chain triglycerides), but not with IntraLipid® or Clinoleic® (long-chain triglycerides), significantly reduced the bradykinin-induced endothelium-dependent relaxations mediated by both nitric oxide (NO) and endothelium-dependent hyperpolarization (EDH). In contrast, Lipidem® did not affect endothelium-independent relaxations to sodium nitroprusside. The endothelial dysfunction induced by Lipidem® was significantly improved by indomethacin, a cyclooxygenase (COX) inhibitor, and by inhibitors of oxidative stress (N-acetylcysteine, superoxide dismutase, catalase) and transition metal chelating agents (neocuproine, L-histidine, desferoxamine). Lipidem® markedly increased the vascular oxidative stress as indicated by increased DHE signal throughout the arterial wall. The present findings indicate that several but not all lipid emulsions induce an endothelial dysfunction in coronary artery rings, involving both blunted NO- and EDH-mediated relaxations. The Lipidem®-induced endothelial dysfunction is associated with increased vascular oxidative stress and the formation of COX-derived vasoconstrictor prostanoids.

Sweet beverages-related acute hyperglycemia and vascular nitric-oxide (NO) endothelial dysfunction: can exercise training be a preventive strategy?

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The main objective of our study was to explore the effects of sweet beverages-related acute hyperglycemia (HG) on vascular endothelial function and the potential role of nitric oxide (NO) signaling pathway in macro- and micro-circulation vascular beds. As several investigators reported that exercise improves NO pathway and endothelial function, we also examined whether regular moderate physical activity could protect vascular endothelial function during hyperglycemia. Laser Doppler blood flow measurements associated to transcutaneous iontophoresis of vasoactives drugs was used to evaluate endothelial function in vivo and in normoglycemic condition (NG) and during an acute hyperglycemic stress (2g/kg of glucose, i.p.; HG). Ex vivo, endothelial function was evaluated on isolated rat aortic rings before and after an hyperglycemic stress (2h, glucose 30mM). The potential role of oxidative stress and NO pathway were evaluated i) pharmacologically by the use, in-vivo, of a non specific antioxidant (N-Acetylcystein, NAC), or of the eNOS cofactor tetrahydrobiopterin (BH4), and ii) with the evaluation of the endothelial NOSynthase (eNOS) activation state (phosphorylation at ser1177) by western blot.

In response to HG an altered endothelium-dependent vasodilation was markedly obvious in microcirculation and to a lesser extent in macrocirculation. Oxidative stress and alteration of the coupling state of eNOS seems to be involved in such result, since the use of NAC or BH4 prevented HG-induced alteration of endothelial function. However, acute hyperglycemic stress has no effect on eNOS phosphorylation state. Finally, chronic aerobic exercise (70% maximal aerobic velocity, 5days/week for 5 weeks) was able to prevent the deleterious effect of HG stress on endothelial function. To conclude, we demonstrated here that in vivo acute HG-related endothelial dysfunction seems to be explained by nitro-oxidative stress, and could be prevented by moderate exercise training.