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

Amissi Said (1), Julie Boisramé-Helms (2), Mélanie Burban (1), Sherezad Rashid (1), Cyril Auger (1), Florence Toti (1), Ferhat Meziani (2), Valérie B. Schini-Kerth (1)

(1) UMR CNRS 7213, Université de Strasbourg, Illkirch, France – (2) NHC, Réanimation Médicale, Strasbourg, France

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 dihydroethidine (DHE). Incubation of coronary artery rings with either Lipidem®, Medique® or Clinoleic® (medium chain triglycerides), but not with Intra-lipid® or Clinoleic® (long-chain triglycerides), significantly reduced the bradykinin-mediated relaxation. The expression of eNOS in aortic sections of CBDL, an increased vascular oxidative stress as indicated by increased vascular oxidative stress and the formation of COX-derived vasoconstrictors and the increased plasma level of pro-inflammatory cytokines in CBDL.

Altogether, these results indicate that PRBJ ingestion prevented the blunted NO- and EDH-mediated endothelium-dependent relaxation in the mesenteric artery of CBDL most likely by preventing the excessive oxidative stress in the arterial wall.

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

Cindy Meziani, Sylvain Battault, Sandrine Gayrard, Cyril Reboul, Gregory Meyer, Guillaume Walther

L’Institut de Biologie Structurale, Université de Lyon, Lyon, France – (3) Hôpitaux Universitaires de Strasbourg, Physiologie et Explo- rations Fonctionnelles, Strasbourg, France – (4) Hôpitaux Universitaires de Lyon, Physiologie et Explo- rations Fonctionnelles, Lyon, France

The main objective of our study was to explore the effects of sweets 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 vasoactive 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 tetrahy- drobiopterin (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. Oxida- tive stress and alteration of the coupling state of eNOS seem 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 exer- cise training.

The Crataegus extract WS1442 retards replicative endothelial senescence by preventing eNOS down-regulation: role of NADPH oxidase- and COX-mediated redox-sensitive expression of p53/p21 and p16

Noureddine Idris Khodja, Thais Porto Ribeiro, Grazielle Silva, Malak Abbas, Marouane Kheloufi, Cyril Auger, Jung-Ok Lee, Valérie B. Schini-Kerth

UMR CNRS 7213, Université de Strasbourg, Illkirch, France

Endothelial cell senescence promoting endothelial dysfunction has been suggested to contribute to the development of age-related vascular disorders. Endothelial senescence is characterized by an irreversible cell cycle arrest involving the p53/p21 and p16 pathways, oxidative stress and down-regulation of endothelial nitric oxide synthase (eNOS). The present study has evaluated whether the Crataegus special extract WS1442, a rich source of polyphenols and a potent activator of eNOS, prevents replicative senescence in cultures of porcine coronary artery endothelial cells, and, if so, to elucidate the underlying mechanism. Replicative senescence was induced by sequential passaging of primary cultures of endothelial cells up to the fourth passage (P4). Senescence was assessed using senescence-associated β-galactosidase (SA-β-gal) activity, the formation of reactive oxygen species (ROS) using dihydroethidine (DHE) by flow cytometry, and the level of protein expression by Western blot anal- ysis. PASSaging of cultures of endothelial cells was associated with a gradual increase in the SA-β-gal activity, the DHE signal and the level of p53, p21 ad