Hypertriglyceridemia but not hypercholesterolemia induces endothelial dysfunction in the rat

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Abstract:
In humans, hypercholesterolemia and hypertriglyceridemia induce endothelial dysfunction and therefore lead to atherosclerosis. In contrast, rats are resistant to atherosclerosis. Here we analyze whether rats respond to hypercholesterolemia and hypertriglyceridemia by developing of endothelial dysfunction.

To induce hypercholesterolemia Wistar-Kyoto (WKY) and spontaneous hypertensive (SHR) rats were fed for 12 weeks with AIN93 diet supplemented with cholesterol (1%) and butter (20%). To induce hypertriglyceridemia Wistar were fed for 8 weeks with AIN93 diet supplemented with 60% fructose. In all experimental groups nitric oxide (NO)-dependent and prostacyclin (PGI₂)-dependent function was assessed in the isolated aorta. Additionally in hypertriglyceridemic rats endothelial function in the isolated mesenteric resistance artery was analyzed.

NO-dependent vasodilation induced by acetylcholine or histamine in aorta of SHR and WKY rats was modestly impaired. Hypercholesterolemic diet fed to WKY and SHR rats induced a rise in total cholesterol and low-density lipoproteins (LDL) cholesterol by 2.5 and 4.5 fold, respectively, but did not further impair NO-dependent vasodilation. Although basal production of PGI₂ in aortic rings from SHR rats was five fold higher than in aortic rings from WKY rats, the hypercholesterolemic diet did not further affect aortic PGI₂ production in either rat strain. Endothelium-independent vasodilation induced by SNAP remained also unchanged. On the other hand, the hypertriglyceridemic diet given to Wistar rats led to a selective 1.5–2 fold elevation of triglycerides that was associated with the impairment of NO-dependent relaxation in aorta as well as in the mesenteric resistance artery. Interestingly, the basal production PGI₂ by aortic rings was not modified by hypertriglyceridemic diet. Again endothelium-independent relaxation induced by S-nitroso-N-acetyl-penicilamine (SNAP) was not affected.

In summary, although in humans both hypercholesterolemia and hypertriglyceridemia are associated with endothelial dysfunction, in rats hypertriglyceridemia only led to the impairment of NO-dependent vasodilation. Hypercholesterolemia did not modify endothelial function even in hypertensive rats that display pre-existing alterations in vasodilator function.

Key words: atherosclerosis, hypertriglyceridemia, hypercholesterolemia, endothelium, NO, PGI₂, spontaneous hypertensive rats (SHR), normotensive Wistar-Kyoto rats (WKY), Wistar rats