COMBINATION THERAPY HAS ADDITIVE EFFECTS TO SIMULTANEOUSLY IMPROVE VASCULAR AND METABOLIC PHENOTYPES OVER MONOTHERAPY IN PATIENTS WITH HYPERCHOLESTEROLEMIA

K. Koh
Cardiology Department, Gachon Medical School, Incheon, Korea

Background: We evaluated simultaneous vascular and metabolic responses to pravastatin and valsartan therapy, alone or in combination, in hypercholesterolemic patients. Methods: Forty-eight hypercholesterolemic patients (23 had metabolic syndrome) were given pravastatin 40 mg and placebo, pravastatin 40 mg and valsartan 160 mg, or valsartan 160 mg and placebo daily during each 2 month treatment period in a randomized, single-blind, placebo-controlled cross-over trial with three treatment arms and two washout periods (each 2 months). Results: When compared with baseline, all three treatment arms improved endothelial dysfunction as assessed by brachial artery flow-mediated dilation (FMD). Of note, FMD improved to a greater extent with combined therapy vs. either monotherapy (P<0.001 by ANOVA). Interestingly, when compared with monotherapy, combined therapy significantly reduced hs-CRP levels to a greater extent (P=0.019 by ANOVA on Ranks). We also observed simultaneous improvement in metabolic phenotypes with all three treatments causing increased plasma adiponectin levels, reduced fasting plasma insulin levels, and increased insulin sensitivity (determined by QUICKI) relative to baseline measurements. For the first time in a statin combination trial, pravastatin combined with valsartan therapy increased plasma adiponectin, lowered fasting insulin, and improved insulin sensitivity in an additive manner when compared with either monotherapy alone (P=0.003, P=0.049, and P=0.049 by ANOVA on Ranks, respectively). Overall, we observed similar results in 23 patients with metabolic syndrome. Conclusions: Pravastatin combined with valsartan improved endothelial function and metabolic phenotypes in an additive fashion in patients with hypercholesterolemia or metabolic syndrome.