GW23-e1177  ROSUVASTATIN COULD MODULATE INSULIN SIGNALLING AND INHIBIT ATHEROSCLEROSIS

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Objectives To provide evidence that rosuvastatin could improve insulin-resistance and inhibit atherosclerosis by modulating insulin-signalling, and whether this effect beyond its plasma cholesterol-lowering effect.

Methods Thirty-two 6-week-old low-density lipoprotein receptor deficient (LDLR-/-) mice were randomised into four groups (n=8 in each group): Normal control group (NC); High fat and high fructose diet group (HFF); HFF plus rosuvastatin group (HFFR); HFFR plus mevalonic acid group (HFFRMA). After 12 weeks, we measured the fasting blood sugar (FBS), fasting insulin (FINS) and total cholesterol (TC); the morphological concentrations of the aorta artery and aorta sinus; the expression of insulin receptor substrate 2 (IRS-2), phosphorylated insulin receptor substrate 2 (P-IRS-2), protein kinase B (AKT, also known as PKB) and phosphorylated protein kinase B (P-AKT) in liver.

Results The HFF diet alone resulted in a plasma FBS concentration of 28.15±1.53 mmol/l and FINS concentration of 1.62±0.07 ng/ml, and administration of rosuvastatin lowered plasma FBS and FINS to 19.99±1.40 mmol/l and 0.79±0.12 ng/ml, while the plasma FBS and FINS levels in HFFR group were partially improved compared to NC group. And administration of rosuvastatin showed a good lipid-lowering effect in HFFR group (33.21±1.12), while this cholesterol-lowering effect of rosuvastatin was significantly reversed by the mevalonic acid in HFFRMA group (39.31±1.57). Furthermore, HFF group had an increase in the morphological concentrations of the aorta artery and aorta sinus, but there was a significant decrease in HFFRMA group and HFFR group. Moreover, there was a high expression of IRS-2, P-IRS-2, AKT and P-AKT in HFFRMA group and HFFR group, but a low expression in HFF group. And there is no significant difference regarding to each afore-mentioned index in HFFR group and HFFRMA group.

Conclusions Our data show that rosuvastatin could improve insulin-resistance and inhibit atherosclerosis in HFF-fed mice by partially reversing the decrease in the insulin stimulated IRS-2/PI3K/AKT pathway in liver, and this effect is independent of its cholesterol-lowering effect.