The effects of metformin and simvastatin on the growth of LNCaP and RWPE-1 prostate epithelial cell lines.

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Abstract

The anti-diabetic drug metformin and cholesterol-lowering statins inhibit prostate cancer cell growth in vitro and have been linked with lowered risk of prostate cancer in epidemiological studies. We evaluated the effects of these drugs on cancerous and non-cancerous prostate epithelial cell lines. Cancer (LNCaP) and normal (RWPE-1) prostate epithelial cell lines were treated with pharmacologic concentrations of metformin and simvastatin alone and in combinations. Relative changes in cell number were measured with crystal violet staining method. Drug effects on apoptosis and cell cycle were measured with flow cytometry. We also measured changes in the activation and expression of a set of reported target proteins of metformin and statins with Western blotting. Metformin decreased the relative cell number of LNCaP cells by inducing G1 cell cycle block, autophagy and apoptosis, and slightly increased cytosolic ATP levels, whereas RWPE-1 cells were resistant to metformin. However, RWPE-1 cells were sensitive to simvastatin, which induced G2 cell cycle block, autophagy and apoptosis, and increased cytosolic ATP levels in these cells. Combination of metformin and simvastatin synergistically decreased cytosolic ATP levels, increased autophagy and instead of apoptosis, induced necrosis in LNCaP cells. Synergistic effects were not observed in RWPE-1 cells. These results suggest, that prostate cancer cells may be more vulnerable to combined growth-inhibiting effects of metformin and simvastatin compared to normal cells. The data presented here provide evidence for the potency of combined metformin and statin, also at pharmacologic concentrations, as a chemotherapeutic option for prostate cancer.

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