Metformin Induces Radiation Sensitivity of Resistant Cells by Influencing Oxidative Stress

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INTRODUCTION: With the high prevalence of type 2 diabetes, the antihyperglycemic medication metformin has become one of the most prescribed pharmacological therapies worldwide. Several researches in recent years accomplished that metformin might be able to reduce cancer incidence and mortality in diabetic patients, but the intriguing fact of which mechanism of action this effect occurs remains unclear. The Warburg Effect demonstrates that proliferative mammalian cells, such as tumors, use the glycolytic pathway to produce ATP even in aerobic conditions, despite oxidative phosphorylation yielding significantly more energy. Cancer cells successfully survive under intense oxidative stress conditions and radiotherapy can eradicate tumors by destroying DNA, increasing ROS levels. Our objective is to investigate how the treatment with both metformin and posterior gamma radiation can affect oxidative stress by using *Saccharomyces cerevisiae* cells as a hypoxic cancer model. **MATERIALS AND METHODS:** *S. cerevisiae* cells were grown in YPGlucose and YPGlycerol medium treated with metformin in different concentrations, ranging from zero to 200 mM. After its subsequent treatment with gamma radiation using ^{60}Co, carbonylation of proteins and lipid peroxidation were the parameters evaluated, compared to not irradiated cells. **RESULTS AND DISCUSSION:** Increase in Metformin concentration decreases cell growth, and affect carbonylation of proteins and lipid peroxidation in yeast. Comparing the metformin and radiation treatment with control situation indicates that protective effects concerning oxidative modifications are induced by radiation on proteins. Apparently, lipid modifications are out of scope of this protection. **CONCLUSION:** Metformin treatment inhibits proliferation of cells. It has a protective effect on cellular proteins, since it prevents protein oxidation. Metformin interferes with redox homeostasis in order to attenuate oxidative stress, mainly on proteins.

Keywords: metformin, cancer, oxidative stress, cancer metabolism, gamma irradiation

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