Metformin interferes with glucose cellular uptake by both estrogen and progesterone receptor-positive (MCF-7) and triple-negative (MDA-MB-231) breast cancer cell lines

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Aim: Transport experiments with 3H-DG, culture growth and proliferation rate assays were performed. This work aimed to investigate the possible interference of metformin with glucose uptake by MCF-7 and MDA-MB-231 human breast adenocarcinoma cell lines as a mechanism contributing to its anticarcinogenic effect.

Introduction: Breast cancer, the most common cancer among women, remains one of the leading causes of mortality among women worldwide. Metformin has been widely used as a treatment for type 2 diabetes for over 40 years. The first report of a reduced risk of developing cancer for diabetic patients treated with metformin was published in 2005. Several mechanisms of action of metformin appear to be implicated in this effect.

Methods: Transport experiments with 3H-DG, culture growth and proliferation rate assays were performed.

Results: Acute (26 min) exposure of MCF-7 cells to metformin significantly inhibited uptake of 3H-deoxy-D-glucose (3H-DG) (maximal inhibition found with metformin 0.5 mM: 27 ± 2% reduction). Chronically (24 h), metformin induced a concentration-dependent increase in 3H-DG uptake (maximal increase observed with metformin 1 mM: 81 ± 15% increase). Acute (26 min) exposure of MDA-MB-231 cells to metformin slightly inhibited uptake of 3H-DG (maximal inhibition found with metformin 1 mM: 10 ± 3% reduction). Chronic (24 h) exposure to metformin significantly increased 3H-DG uptake by MDA-MB-231 cells (maximal increase observed with metformin 1 mM: 30 ± 8% increase).

Chronic (24 h) exposure of both cell lines to metformin (1 mM) decreased culture growth/cell mass; in contrast, it increased cell proliferation rates. Combination of metformin (1 mM) with the facilitative glucose transporter (GLUT) inhibitor kaempferol (30 μM) did not result in a more marked effect on culture growth and cell proliferation rates.

Conclusion: Summarizing, chronic exposure of MCF-7 and MDA-MB-231 cells to metformin induces a marked increase in glucose uptake, associated with an anticarcinogenic effect of the drug. We suggest that the increase in glucose uptake is a compensatory mechanism to cellular energy depletion induced by metformin.

Acknowledgements: This study was supported by Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Portugal (Plano estratégico UID/BIM/04293/2013).