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The Effects of Short Chain Fatty Acids (Butyrate) on the Permeability, Cell Viability, and Inflammatory Changes Due to Oxidative Stress in Lung Epithelial Cells

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Objectives: At present, there is no successful treatment, yet, in the treatment of chronic airway diseases such as chronic obstructive pulmonary disease (COPD) and asthma, which are important causes of mortality and morbidity. In the pathogenesis of these diseases, there is an increased oxidative stress, disrupted permeability, apoptosis and inflammation in the airway epithelium. It has been showed that short-chain fatty acids such as butyrate have a regulatory role in cell physiology, as well as anti-inflammatory effects at cellular level. The objectives of this study were to investigate the effects of hydrogen peroxide (H_2O_2) and butyrate on permeability and cell viability of airway epithelial cell cultures.

Methods: Bronchoalveolar carcinoma cells (A549) were proliferated on semi-permeable cell culture inserts, and treated with 0, 100, 300, 600 µM H_2O_2or 0.3, 1, 3 mM butyrate. Cell culture permeability was assessed by measuring trans-epithelial electrical resistance (TEER) at T0, T2, T4, T6 and T24 hours. Cell viability was determined at T24 and T48 hours with the staining method that is based on the uptake and reduction of the 3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) by mitochondrial enzymes of viable cells.

Results: H_2O_2 at 100 µM concentration caused a significant increase in TEER at 6. hour (median: 129.8%, $p<0.05$), when compared with the control group (median: 115.3%). On the other hand, 600 µM H_2O_2 caused a significant decrease in TEER at 24. hour (medians: 124.6% vs 105.6%, $p<0.01$). Butyrate did not cause any changes in the TEER of cell cultures. Cell viability data showed that all applied H_2O_2 concentrations (100-600 µM) significantly decreased the cell viability at T24 and T48 hours, as compared with the control group ($p<0.01$). The highest concentration of butyrate (3 mM) significantly suppressed the cell viability at T24 hours (median: Optical density (OD) 0.5675 vs 0.3275, $p<0.01$), while lower doses had no effect.

Conclusion: These findings show that H_2O_2 can decrease A549 cell viability, while increasing the cell permeability, and that butyrate can be cytotoxic at higher doses, while having no effect on the cell viability at lower doses. For future studies, it would be plausible to investigate whether butyrate can prevent detrimental effects of H_2O_2 on air way epithelial cells.

Keywords: Lung epithelial permeability, cell viability, A549, butyrate, short chain fatty acids, oxidative stress