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Assessment of improvement in epithelial barrier function using prolyl hydroxylase inhibitor DMOG in murine model of colitis

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Background: Ulcerative colitis is one of two forms of inflammatory bowel disease characterised through relapsing and debilitating symptoms such as bloody diarrhoea, weight loss and abdominal pain. Worldwide prevalence of ulcerative colitis continues to increase while the aetiology remains unclear. Dimethyloxalylglycine mechanism of action is through inhibition of prolyl hydroxylase (PHD) resulting in stabilisation of hypoxia-inducible factors (HIF). Dextran Sodium Sulphate (DSS)-induced colitis in murine models replicates the destruction caused by ulcerative colitis allowing evaluation of the therapeutic effects of dimethyloxalylglycine.

Objectives: This project assesses the effects DSS-induced colitis has on epithelial cells, goblet cells and neutrophils, hypothesising dimethyloxalylglycine will improve the epithelial barrier function in a murine model of DSS-induced colitis by ameliorating both epithelial and goblet cell counts, while diminishing neutrophil infiltration.

Methods: Therapeutic effects of dimethyloxalylglycine were assessed using 16 female mice, originating from the C57BL/6 strain, divided into four groups; a negative control group given water, a positive control group provided with 2.5% DSS w/v and two treatment groups; one with DSS 2.5% w/v and 0.1mg DMOG and the other with DSS 2.5% w/v and 1mg DMOG. Quantitative histological evaluation of epithelial cells, goblet cells and neutrophils provided data for statistical analysis using student unpaired t-tests. Results with a P value < 0.05 were considered significant.

Results: Therapeutic effects of dimethyloxalylglycine were visible through the histological evaluation with unpaired t-tests demonstrating statistically significant differences in goblet cells (P=0.0234,*), neutrophils (P=0.0054,**) and inflammatory score (P=0.0010, ***) while epithelial cells showed no significant difference (P=0.0809, ns). This statistical analysis is respective of 1mg DMOG.

Conclusions: Dimethyloxalylglycine treatment promotes regeneration of the epithelial barrier through increased epithelial and goblet cell counts and reduction of neutrophil infiltration subsequently improving inflammatory score. Therapeutic benefits of dimethyloxalylglycine as a management for ulcerative colitis are highlighted by this study.

Biography

Mia Coffey is a third-year medical student from Northern Ireland, currently pursuing her studies at the University of Nottingham, England. As part of her five-year medical program, she also completed a bachelor's degree in Medical Sciences, where her research focused on inflammatory bowel disease, with particular emphasis on ulcerative colitis and the exploration of a potential therapeutic agent. Passionate about advancing patient care, she is eager to follow the progress of emerging treatments for ulcerative colitis over the coming years. As she continues her medical training and prepares for her career as a doctor, she aspires to contribute to improving the quality of life for patients affected by this challenging condition.

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