MEDICAL THERAPIES AND PHARMACOLOGY

GLUCOCORTICOIDS DISTURB SKIN BARRIER FUNCTION VIA ACTIVATION OF MINERALOCORTICOID RECEPTOR AS WELL AS GLUCOCORTICOID RECEPTOR

H Lee [1] - Ej Choi [2] - Ej Kim [1] - Ed Son [2] - Tr Lee [2] - Eh Choi [1]

Yonsei University Wonju College Of Medicine, Department Of Dermatology, Wonju, Republic Of Korea [1] - Amorepacific Corporation, Basic Research & Innovation Division, R&d Unit, Yongin, Republic Of Korea [2]

Introduction: Glucocorticoids (GC) deteriorates skin barrier as well as wound healing. In skin where 11β-hydroxysteroid dehydrogenase 2 which prevents GC from binding to mineralocorticoid receptor (MR) is deficient, GC can bind to MR as well as GC receptor (GR). MR has been reported implicated in GC-induced delayed wound healing and epidermal atrophy.

Objective: To test whether GC binds to MR and contributes to skin barrier dysfunction and thus MR antagonism can prevent GC-induced skin barrier dysfunction.

Material and Methods: To elucidated MR expression in epithelial cells, Western blot (WB) and immunofluorescence (IF) stain were performed using human oral mucosa and foreskin. In healthy young adults (n=6), skin barrier function was measured after application of topical corticosteroid either with 5% spironolactone (MR antagonist) cream or vehicle on each forearm. Normal human epidermal keratinocytes (NHEKs) were treated with cortisol and the expression and intracellular localization of GR and MR were examined by WB and IF. To investigate the roles of GR and MR, after treating cortisol and mifepristone (GR antagonist) or eplerenone (MR antagonist) to NHEKs, keratinocyte differentiation markers were evaluated.

Results: MR expression was observed in oral epithelial cells and epidermal keratinocytes by WB and IF stain. In the topically corticosteroid treated skin, co-treatment of topical MR antagonist improved stratum corneum integrity (p=0.08) and barrier recovery rate (p=0.12) compared to vehicle albeit without statistical significance. In NHEKs, protein expression of GR but not MR was decreased by cortisol. In contrast, cortisol induced the nuclear localization of both GR and MR, which were inhibited by mifepristone and eplerenone, respectively. Cortisol decreased the expression of keratinocyte differentiation markers, which was recovered by eplerenone.

Conclusion: GC binds to MR as well as GR and contributes to skin barrier dysfunction. Therefore, MR antagonist as well as GR antagonist might prevent GC-induced skin barrier dysfunction.