Evaluation of Glucocorticoid-induced Skin Atrophy on Full-thickness Skin Models

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Glucocorticoids (GCs) are the most widely used class of anti-inflammatory drugs, but their therapeutic use is limited by serious side effects, with skin atrophy being the most prominent limitation. Thus, determining the atrophogenic potential of novel compounds is of great importance for drug development. Currently, there are no predictive *in vitro* models available. The aim of the present study was to establish an *in vitro* model for the evaluation of GC-induced skin atrophy by quantification of collagen synthesis and degradation upon topical treatment. In initial experiments primary human fibroblasts and keratinocytes were pretreated with TNF-ÿ to induce an inflammatory response followed by incubation with GCs for 72 h. Prednicarbate (PC) and clobetasol propionate (CP) were selected as a mid- and high-potency GC, respectively. Quantification of gene expression by real-time RT-PCR showed a strong downregulation of COL1A1 and COL3A1 mRNA expression by CP in fibroblasts, whereas PC only minor affected COL3A1. No effect was observed in keratinocytes. Analysis of IL-6 release by ELISA confirmed the anti-inflammatory effects. After the successful establishment of monitoring collagen expression in monolayer cultures, GCs were applied topically to full-thickness skin models (EpidermFT, Mattek™) for 7 days. Under inflammatory conditions, CP again downregulated collagen expression, whereas PC even slightly increased collagen expression. Accordingly, histological analysis revealed a reduction of the epidermal thickness in the CP-treated samples, thus correctly reflecting the atrophogenic potential observed *in vivo.* In summary, the results indicate that skin models appear to be a promising alternative method to determine and predict the atrophogenicity of GCs.