Differential effects of synthetic glucocorticoids on gene expression levels of IL-2 and glucocorticoid-induced leucine zipper (GILZ) in peripheral blood mononuclear cells

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Glucocorticoids (GCs) exert a wide variety of effects in the human body. Many of these effects are mediated by glucocorticoid receptor (GR) induced changes in the level of expression of GC-regulated genes. The anti-inflammatory and immune-suppressive effects of glucocorticoids are also used in therapeutic settings. However, there exists a considerable inter-individual variation in GC-sensitivity, resulting in a variable response at the level of both beneficial and side effects. In this study, we have tried to assess individual GC sensitivity by measuring the effects several clinically used GCs directly on gene expression in human peripheral blood mononuclear cells (PBMCs). Because GCs exert both stimulatory and inhibitory effects on gene expression through different mechanisms, we determined the effects of GCs on transrepression of the interleukin-2 (IL-2) gene and transactivation of the glucocorticoid-induced leucine zipper (GILZ) gene by means of real-time RT-PCR. We saw a clear difference in potencies of the various GCs tested. Interestingly, the potency of the GCs was not the same for transactivation and transrepression, suggesting a differential effect. We were also interested whether these *in vitro* outcomes could predict *in vivo* effects of GCs. For this purpose, fifteen healthy volunteers underwent a 0.25 mg dexamethasone suppression test (DST), while determining GILZ and IL-2 expression levels in their PBMC incubated with hydrocortisone, dexamethasone (DEX), budesonide and prednisolone. Again, differential effects on transactivation and transrepression were seen. In DEX-stimulated PBMCs, lower GILZ expression levels corresponded to a lower response to DEX in the DST ($P=0.043$). However, this was not observed with IL-2 expression levels. Further, correlations were found between hydrocortisone and DEX ($P=0.017$), budesonide ($P=0.029$) and prednisolone ($P<0.01$) regarding GILZ expression levels, and between hydrocortisone and DEX ($P=0.05$), budesonide ($P<0.01$) and prednisolone ($P<0.01$) regarding IL-2 expression levels.

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