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Persistent glucocorticoid resistance in systemic lupus erythematosus patients during clinical remission

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ABSTRACT. Glucocorticoids (GCs) are key drugs in the treatment of systemic lupus erythematosus (SLE). GC dose reduction during remission is related to disease activity, GC dose used, length of treatment, and individual GC sensitivity. We compared GC receptor α (GRα) isoform and nuclear factor kappaB (NF-κB) messenger RNA quantitation and *in vivo* GC sensitivity between SLE patients during remission and healthy controls. We performed a cross-sectional study of 19 women aged 22-49 years, including 9 SLE patients in clinical remission taking ≤5 mg prednisone and 10 matched controls. We evaluated GC sensitivity using 2 cortisol suppression tests: a very-low-dose intravenous dexamethasone suppression test (VLD-IV-DST) and a low-dose oral dexamethasone suppression test. GRα and NF-κB mRNA were quantified using real-time polymerase chain reaction. Although basal cortisol and adrenocorticotropic hormone levels were similar between the groups, the percentage of cortisol reduction after the VLD-IV-DST was 56% lower in SLE patients than in controls (P = 0.014). GRα and NF-κB

gene expression levels were similar between the groups. The low-dose oral dexamethasone test caused intense cortisol suppression in all individuals, limiting the ability of this test to discriminate individual GC sensitivity. A positive correlation was found between the extent of cortisol suppression *in vivo* (VLD-IV-DST) and the number of days elapsed since the last flare of lupus activity. Despite clinical remission, SLE patients displayed partial GC resistance recognized by the VLD-IV-DST. The mechanism of this resistance is unrelated to altered GRα and NF-κB mRNA expression.

Key words: Cortisol; Dexamethasone; Glucocorticoid sensitivity; Systemic lupus erythematosus

