THE EFFECTS OF GLUCOCORTICOIDS ON OXYGEN DERIVED FREE RADICAL GENERATION: POSSIBLE IMPLICATIONS WITH NFκB AND IκB

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ABSTRACT

Glucocorticoids(GCs) such as hydrocortisone and dexamethasone, have been administered for many years as potent agents able to suppress the inflammatory response yet their mechanism of action is poorly understood. I investigated whether GCs inhibit oxygen derived free radical generation (OFR) when given systemically. I administered a single dose of 100 mg of hydrocortisone for 6 subjects. Blood samples were obtained prior to and sequentially at 0,30,60,120 min and 4 hrs after injection. Following the 100 mg of hydrocortisone, fMLP (an inducer of free radicals; mainly superoxide anions) induced oxygen derived free radical generation fell at 1 hr and gradually recovered to the basal level at 8 hr. Recently, in vitro investigations have pointed in the direction of two transcription factors: Nuclear Factor Kappa B (NFκB) and Inhibitory Factor Kappa B (IκB), as the main agents in the anti-inflammatory response mediated by glucocorticoids. NFκB encodes for various inflammatory products such as cytokines, interleukin molecules, free radicals, intercellular adhesion molecules (ICAM). IκB, antagonistically, inhibits the production of these inflammatory products. Therefore, I investigated the effect glucocorticoids have on NFκB and IκB induction in correlation with the results from the free radical generation study. Western blot analysis, performed on MNC homogenates isolated from blood samples at the above mentioned time points, showed that NFκB levels remained the same at all time points whereas IκB levels peaked at 60 min. Therefore, indirectly, GCs might be involved in OFR production by MNC via NFκB/IκB mediated mechanisms.