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HMGB1 DANGER SIGNALING MODULATES T CELLS PHENOTYPE AND CYTOKINE PROFILE IN RESPONSE TO REDOX STATUS IN DEPRESSED PATIENTS. AN EFFECT ON GLUCOCORTICOID RECEPTOR FUNCTION

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Objectives: We aimed to study HMGB1, pro- and antioxidant status alongside with T cells phenotype and Th1 and Th17 proinflammatory cytokine profiles in depressed patient. We also investigated the glucocorticoid response.
Methods: Blood was collected from patients diagnosed with recurrent depressive disorder (rDD) (N=15) and from healthy controls (N=19). We measuredplasma hydrogen peroxide (H_2O_2) and reduced glutathione (GSH) , malondialdehyde (MDA) levels as well as SOD1, GPx, GR activities in red blood cells. HO1 and NOX4 levels in plasma were also assayed. IL-2, IL-6, IL-8, IFN-g, TNF-a, IL-17, HMGB1, neopterin and cortisol were analyzed in sera. Further, we examined surface phenotype expression of T regulatory and T effector cells with flow cytometer. The glucocorticoid response was measured by dexamethasone-induced inhibition of IL-6 produced by LPS-stimulated peripheral blood.
Results: We observed pro- and antioxidant imbalance in depressed patients expressed by significant changes in the enzyme activities, increased MDA, decreased GSH, increased H_2O_2. Shifted Th1/Th17 cytokine ratios, increased Treg/Teffector cells ratio and increased levels of neopterin were also detected. Moreover, we revealed a distinct role of HMGB1 in maintaining cytokine and Treg/Teffector cells balance in depressed patients. HMGB1 remained also in relation with oxidant potential of the blood. The important role of IL-17 and inhibitory effect of MDA on glucocorticoids response was also revealed.
Conclusions: Strong immunomodulatory role of HMGB1 might be related to the change of its activity caused by redox imbalance in depressed patients. The shifted immune balance alongside with prooxidative environment modulates glucocorticoid response in these patients.

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