Endotoxin Tolerance is Associated with Increased S100A8 and S100A9 mRNA Expressions

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Abstract

Background: Septic syndromes are the leading cause of mortality in intensive care units and are characterized by the development of a stage of profound immunosuppression affecting both innate and adaptive immunity. The intensity and duration of these immune dysfunctions are associated with delayed mortality and risk of nosocomial infection after septic shock. We recently showed that S100A8 and S100A9 (two alarmins produced by monocytes) mRNAs were increased after septic shock and that delayed S100A9 mRNA increase predicted hospital-acquired infection in patients. Our aim was to investigate the regulation of S100A8 and S100A9 mRNA expressions in ex vivo models mimicking immune dysfunctions observed in septic shock patients.

Methods: Peripheral blood mononuclear cells were isolated from healthy volunteers and stimulated once with LPS (0 to 200 ng/ml) overnight or twice (2 ng/ml and 100 ng/ml) over 48h. This model of double LPS stimulation is known to induce endotoxin tolerance ex vivo. TNFα, IL-10, S100A8 and S100A9 mRNAs expressions were measured using RT-qPCR.

Results: We observed that a single stimulation with LPS increased TNFα, IL-10, S100A8 and S100A9 mRNA expressions in a dose-dependant manner. Importantly and as expected, our model of endotoxin tolerance was associated with decreased TNFα mRNA level and increased IL-10 mRNA expression. Interestingly, in this model, we observed a significant increase of S100A8 and S100A9 mRNA levels.

Conclusion: In this study, we observed that LPS stimulation increased S100A8/A9 mRNA levels. Importantly and as observed in septic shock patients, this increase was even more important in our model of endotoxin tolerance. As this increase was associated with increased IL-10 production and as the literature suggested a role for IL-10 in the regulation of S100A8 and S100A9 expressions, we plan to evaluate the role for this cytokine in S100A8 and S100A9 mRNAs expression regulation in our model.