CYTOKINES HARMFUL EFFECT ON RBCS VIABILITY: PRELIMINARY RESULTS FOR ERYPTOTIC MECHANISM IN SEPSIS

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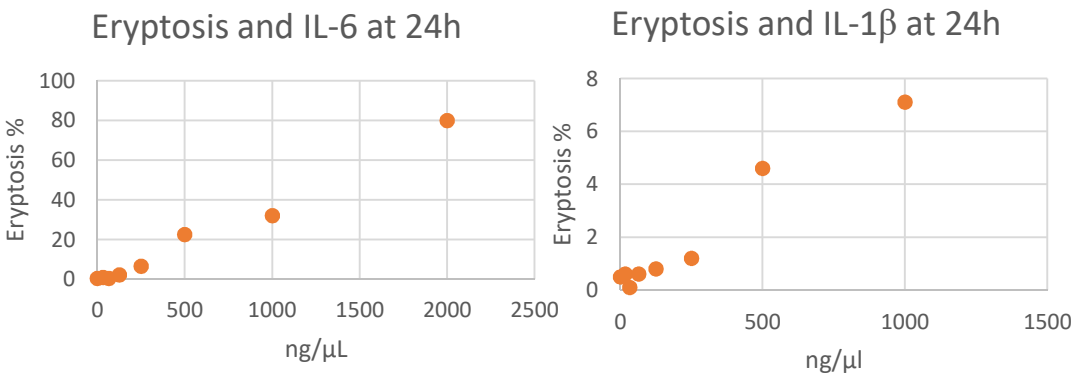
Background: Sepsis is a health issue that affects millions of people worldwide. It was assumed that erythrocytes were affected by sepsis. Erythrocytes (RBCs) are enormously sensitive cells and have a greatly specialized and organized membrane structure, which interacts and reacts to xenobiotic and endogenous elements. RBCs undergo programmed cell death, comparable to apoptosis, known as eryptosis. Triggers of eryptosis include increased cytosolic Ca(2+) concentration, oxidative stress, inflammation, and several uremic toxins.
The aim of this study was to evaluate eryptosis levels in healthy RBCs treated with different concentrations of IL-6 and IL-1β, present in septic plasma, at different time points.

Methods: We exposed healthy whole blood to different increasing concentrations of IL-6 and IL-1β (IL-6: 2000-1000-500-250-125-62.5-31.25-0 ng/µl; IL-1β: 1000-500-250-125-62.5-31.25-15.63-0 ng/µl. We used untreated RBCs as a negative control. Eryptosis (= Phosphatidylserine (PS) exposure at RBC surface) was estimated using flow cytometric analyses.

Results: The cytotoxic effect of cytokines was studied *in vitro* on RBCs at 4, 8, and 24 hours. RBCs incubated with IL-6 and IL-1β demonstrated a significant increase in eryptosis. Cytofluorimetric analysis of eryptosis highlighted significantly higher cell death rates in RBCs incubated with higher concentrations of both cytokines compared with other concentrations and untreated cells ($p < 0.05$). Figure 1 describes eryptosis inducted by IL-6 and IL-1β *in vitro* exposure at different concentrations and at different time points (Figure).



Conclusion: To the best of our knowledge, the levels of eryptosis and its association with inflammation and cytokines have not been yet investigated. In this study, we evaluated relationship between eryptosis and unconventional inflammatory indices. Our data indicate that cytokines have a harmful effect on RBCs viability and cause eryptosis. Further studies are necessary to validate these results and associate abnormal eryptosis during sepsis with inflammation and cytokine levels.