Correlation Between Cytokine Levels and Lung Injury in the Syrian Hamster (Mesocricetus Auratus) Covid-19 Model

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Abstract : The level of major cytokines in the blood of patients with COVID-19 varies greatly depending on age, gender, duration and severity of infection, and comorbidity. There are two clinically significant cytokines, IL-6 and TNF-α, which increase in levels in patients with severe COVID-19. However, in a model of COVID-19 in hamsters, TNF-α levels are unchanged or reduced, while the expression of other cytokines reflects the profile of cytokines found in patients' plasma. The aim of our study was to evaluate the relationship between the level of cytokines in the blood, lungs, and lung damage in the model of the Syrian hamster (Mesocricetus auratus) infected with the SARS-CoV-2 strain. The study used outbred female and male Syrian hamsters (n=36, 4 groups) weighing 80-110 g and 5 months old (protocol IACUC, #4, 09/22/2020). Animals were infected intranasally with the hCoV-19/Kazakhstan/KazNAU-NSCEDI-481/2020 strain and euthanized at 3 d.p.i. The level of cytokines IL-6, TNF-α, IFN-α, and IFN-γ was determined by ELISA MyBioSourse (USA) for hamsters. Lung samples were subjected to histological processing. The presence of pathological changes in histological preparations was assessed on a 3-point scale. The work was carried out in the ABSL-3 laboratory. The data were analyzed in GraphPad Prism 6.00 (GraphPad Software, La Jolla, California, USA). The work was supported by the MES RK grant (AP09259865). In the blood, the level of TNF-α increased in males (p=0.0012) and IFN-γ in males and females (p=0.0001). On the contrary, IFN-α production decreased (p=0.0006). Only TNF-α level increased in lung tissues (p=0.0011). Correlation analysis showed a negative relationship between the level of IL-6 in the blood and lung damage in males (r -0.71, p=0.0001) and females (r-0.57, p=0.025). On the contrary, in males, the level of IL-6 in the lungs and score is positively correlated (r 0.80, p=0.01). The level of IFN-γ in the blood (r -0.64, p=0.035) and lungs (r-0.72, p=0.017) in males has a negative correlation with lung damage. No links were found for TNF-α and IFN-α. The study showed a positive association between lung injury and tissue levels of IL-6 in male hamsters. It is known that in humans, high concentrations of IL-6 in the lungs are associated with suppression of cellular immunity and, as a result, with an increase in the severity of COVID-19. TNF-α and IFN-γ play a key role in the pathogenesis of COVID-19 in hamsters. However, the mechanisms of their activity require more detailed study. IFN-α plays a lesser role in direct lung injury in a Syrian hamster model. We have shown the significance of tissue IL-6 and IFN-γ as predictors of the severity of lung damage in COVID-19 in the Syrian hamster model. Changes in the level of cytokines in the blood may not always reflect pathological processes in the lungs with COVID-19.

Keywords : syrian hamster, COVID-19, cytokines, biological model
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