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EFFECTS OF NATIVE, ACTIVATED AND PRIMED MESENCHYMAL STROMAL CELLS ON HEMATOLOGICAL PARAMETERS, ORGAN MASS AND IMMUNE CELL INFILTERATION IN EXPERIMENTAL SEPSIS

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Relevance. Sepsis remains as one of the most important causes of morbidity and mortality globally, mainly due to disrupted inflammatory host response to infection that results in several vital organ malfunction. Mesenchymal stromal cells (MSCs) have been identified as a potential biologic therapy owing to their immunomodulatory, anti-inflammatory, and tissue-regenerative effects. Current studies suggests that preconditioning MSCs can enhance their therapeutic efficiency, however, comparative data on how different activation and priming strategies affect hematological profiles, organ mass, and immune cell trafficking in sepsis remain undefined.

Aim: to evaluate the effects of native, activated, and primed MSCs on hematological parameters, relative organ mass, and immune cell infiltration.

Materials and methods. Rats were subjects to sepsis, followed by intravenous injections of either native stromal cells, activated stromal cells (exposed to TLR agonists), or primed stromal cells (exposed to inflammatory cytokine). The sepsis without treatment group acted as the control. Parameters, including red blood cell (RBC) count, hemoglobin, hematocrit, white blood cell (WBC) differential count, thrombocit (PCT), mean corpuscular hemoglobin concentration (MCHC) and others were analyzed. The relative masses of the organs such as lungs, hearts, liver, kidney and spleen were calculated. To confirm immunological cell infiltration, histological examinations of lung and spleen tissues was performed using Romanowsky Giemsa stain and May-Grünwald staining methods. The results indicating changes in animal parameters compared to the control group were considered statistically significant at $p<0.05$. The results indicating changes in animal parameters compared to the native stromal cell group were considered statistically significant at $p^*<0.05$.

Results and their discussion. The most pronounced hematological changes were caused by the primed stromal cells. The changes were significant decrease in mean RBC count ($p=0.0020$), hemoglobin ($p=0.0045$), and hematocrit ($p=0.0220$ (treated and untreated), $^*p=0.0021$ (activated and not activated), as well as elevated thrombocyte count ($p=0.0322$, $p^*=0.0149$) and PCT ($p=0.0166$, $p^*=0.0066$). The activated stromal cells caused a significant increase in mean MCHC compared to control group ($p=0.0005$) and native cells ($p^*<0.0001$). All treatment groups showed increased neutrophil percentage and decreased lymphocyte percentage relative to the control group. When considering organ mass, activated cells caused elevations in the relative mass of lungs ($p=0.0405$), while both activated and primed cells significantly increased the mass of heart ($p=0.0072$ and $p=0.0121$, respectively) and mass of spleen ($p^*=0.0295$ and $p^*=0.0024$) compared to native stromal cells. Histological examination using Romanowsky Giemsa (in May-Grünwald modification) staining methods confirmed that the significant increase in masses of spleen and liver was due to marked infiltration of lymphocytes, neutrophils and monocytes into the tissues of these specific organs. These practical findings demonstrate that preconditioned MSCs exhibit improved immunoregulatory effects thus enhancing the immune cell accumulation in selective organs.

Conclusions. These primed and activated stromal cells represent hematological and organ-protective effects in sepsis compared to native cells. The effectiveness of MSC-based therapies can be estimated through numerous important findings including: a significant increase in relative masses of spleen and liver and elevated levels of RBC, hemoglobin levels, hematocrit levels, monocytes, lymphocytes and neutrophils. These measurements of organ mass in conjunction with histological evidence of monocyte and lymphocyte infiltration allow for an overall estimate of MSC therapy performance. These results suggest that developing different priming strategies optimizes the therapeutic potential of the MSCs in managing septic patients.