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Study of immunomodulatory effects of mesenchymal stem cell-derived exosomes in a mouse model of LPS induced systemic inflammation

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ABSTRACT

Background: Sepsis is a debilitating systemic inflammation that resulted from infection or injury. Despite many advances in treatment, the resulting mortality rate has remained high due to increasing antibiotic resistance and aging communities. The present study investigated the effects of stem cell-derived exosomes in a mouse model of LPS-induced systemic inflammation.

Materials and methods: To induce sepsis, the LPS model was used. Mice were divided into three groups: normal, patient group (LPS + PBS), and treatment group (LPS + exosome). The treatment group received an intravenous exosome 1 h after induction of the model. Patient and treatment groups were sacrificed at 4, 6, 24, and 48 h after induction of the model, and their tissues were isolated. Blood samples were taken from animal hearts to perform biochemical and immunological tests. The study results were analyzed using Graph Pad Prism software version 9.

Results: Mesenchymal stem cell-derived exosomes decreased serum levels of ALT and AST liver enzymes, decreased neutrophil to lymphocyte ratio (NLR), and improved kidney, liver, and lung tissue damage at 4, 6, and 24 h after model induction. At 24 h, the exosomes were able to reduce serum urea levels. This study revealed decreased levels of inflammatory cytokines such as IL-6, IL-1β, and TNF-α after exosome injection.

Conclusion: Our findings suggest that treating mice with stem cell-derived exosomes can ameliorate the destructive effects of inflammation caused by sepsis by reducing inflammatory factors and tissue damage.

1. Introduction

Sepsis is a heterogeneous syndrome caused by systemic dysregulation of inflammatory responses to localized severe infection, leading to tissue injury, multiple organ dysfunction, and death [1]. Although significant advances in understanding the pathophysiology of sepsis have increased over the last few decades, the precise mechanisms are still widely disputed [2–4]. Excessive inflammation is thought to be critical in eradicating causal pathogens. Still, it also leads to complicated pathophysiology associated with greater systemic secretion of both pro-inflammatory and anti-inflammatory mediators, which is involved in bystander attacks on principle tissues, causing damage in several organs, hemodynamic impairments, and autonomic nervous system failure [5,6]. Almost all sepsis patients experience acute lung injury, heart failure, leukocyte migration, apoptosis, and multiple organ dysfunction syndrome (MODS) [7]. Despite modern pharmacological regimens, the ongoing development of new antibiotics, health education initiatives, the promotion of preventive care, and infection-control guidelines, sepsis remains one of the biggest causes of mortality in hospitalized patients globally, particularly given the population's aging and the advent of antibiotic resistance [8]. Consequently, innovative and efficient approaches focused on preventing rapid organ failure during sepsis that would significantly impact the disease's probable progression to mortality.

The growing interest in the therapeutic efficacy of mesenchymal stem cells (MSCs) in preclinical studies has recently been established based on their immunomodulatory capabilities and paracrine actions [9]. MSCs are stimulated by pro-inflammatory cytokines secreted by

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