

Apoptotic Cell–Based Therapy: Is it a Novel Therapeutic Option for Trauma Hemorrhagic Shock?

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Introduction

Trauma induced-hemorrhagic shock (HS) is the major leading cause of death after trauma. Latest study reported that estimated 1.9 million lives worldwide per year [1]. Treatment of trauma induced hemorrhagic shock is limited. Although last decades improved trauma care system and increased survival rate of HS. Blood and their components and control massive hemorrhage used to cornerstone of management of THS. Approximately 66.7 percent death results from other than massive hemorrhage. Excessive massive hemorrhage associated with dysregulation of immune system leads to susceptibility to infection., sepsis, MOF and death, Figure 1 [2].

Previous study reported that excessive release of cytokine such as interleukin (IL)-1 β , IL-6, IL-10, interferon γ (INF γ), and others are involved in suppression of immune system. Suppression of immune system is characterized by decreased T- and B-cell function. The function of splenic dendritic cells and macrophage antigen presenting function were depressed following THS. Suppressed immune system or its complication can be reversed by Apoptotic Cell–Based Therapy (ACBT) [3-4]. Previous literature reported that ACBT pro and anti-inflammatory cytokine result modulation of immune system. Previous clinical trial with anti-inflammatory that showed there is no significant improved on trauma and found unfavorable results. Poor outcome has been reported when treated with leukoreduced blood, anti-CD18, anti-L-selectin, INF γ , and statins. Previous literature reported that treatment with hydrocortisone in severe trauma reduced the risk of hospital acquired infection. However, treated with intravenous (IV) corticosteroid increased the mortality rate in head injury trial. And also treated with IV immunoglobulin reduced the risk of secondary infection after trauma but there is no improved in outcome of mortality [4-6].

Apoptotic Cell Therapy in trauma induced hemorrhagic Shock is an emerging research area that explores how programmed cell death (apoptosis) can be harnessed to control inflammation and improve survival after severe blood loss. Recent studies reported that Apoptotic cells act as immunomodulatory function associated with clearance of apoptotic cell by macrophage via through phagocytosis. Results ACBT is used to prevent or treat inflammatory disorder. Mevorach et al reported that a single infusion of donor mononuclear early apoptotic cells was beneficial

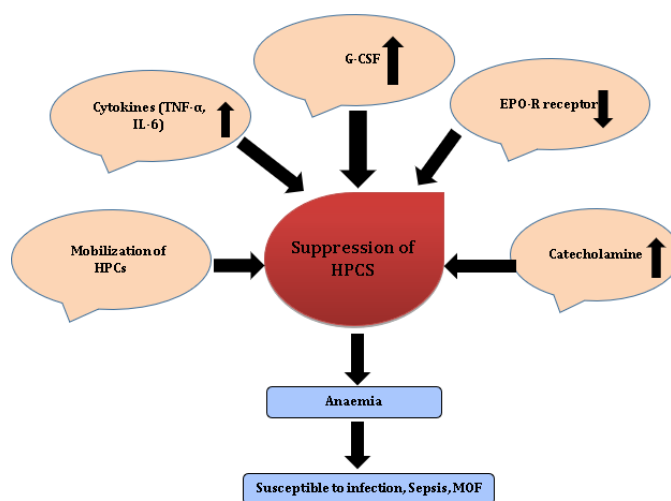


Figure 1: Diagrammatic representation of suppression of HPCs.

and effective for preventive preventing graft-vs-host disease (GVHD) after hematopoietic cell transplantation in patients with hematologic malignancies, with a good safety profile [6]. Administrated with apoptotic cell improved joint inflammation may even have therapeutic effects on arthritis [7]. Moreover, ACT were also tested in sepsis and coronavirus pandemic. In animal model, treated with apoptotic cells to rats in hemorrhagic shock reduced cytokine level. The uniform decrease in pro-inflammatory cytokines shows a potential for this novel therapy and other immunomodulatory strategies, in reducing inflammation derived multiorgan failure and immunosuppression in patients in hemorrhagic shock, figure 2.

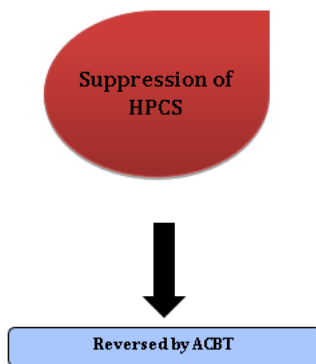


Figure 2: Suppression of HPCs reversed by ACBT.

Based on the previous studies reported that ACBT is an emerging, safe, and innovative treatment approach that uses early apoptotic cells to induce immune tolerance and resolve inflammation. ACBT is used as a therapeutic potential for trauma hemorrhagic shock using animal model. but still remain its role of ACBT in T/HS patients. ACBT, may prevent the body’s overreaction to blood

loss and reduce organ damage—offering a promising but still developing treatment strategy.

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