Harnessing Human Umbilical Cord-Derived Hydrogel and MSCS for Effective Hypoxic Wound Treatment

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ABSTRACT

Hypoxia is the critical factor observed in almost all pathological conditions that affect wound healing process. Comorbid health conditions like diabetes (Zhang *et al*., 2024), cirrhosis (Lin *et al*., 2024), vascular diseases etc., or bacterial infections at the wound site (Dashti *et al*., 2024) all exhibit elevated levels of reactive oxygen species (ROS) in the wound microenvironment. Oxidative stress results in prolonged inflammation, apoptosis, and hampers neovascularization. This leads to poor wound closure and delayed wound healing (Ren *et al*., 2024). Regenerative medicine could be the potential therapeutic approach to address hypoxic condition hence delayed wound healing as studies showed that isolate mesenchymal stem cells (MSCs) have immune modulating properties and have the potential to differentiate into the respective tissue cells (Fuchs *et al*., 2023). Besides, tissue derived bio-scaffolds due to their biocompatibility and extracellular matrix (ECM) composition support the localized delivery and survival of transplanted cells (Dussoyer *et al*., 2020).

Objective: This study aims to create a hydrogel from human umbilical cord (hUC), to isolate MSCs from hUC tissue and to investigate the synergistic effect of MSCs and the hydrogel for hypoxic wound treatment.

Methodology: The hydrogel was prepared through the decellularization of hUC tissue. Cells (MSCs) were isolated from the hUC after obtaining informed consent. A full-thickness hypoxic wound was created and characterized based on histological analysis including H & E, and Masson's trichrome staining and by immunohistochemistry. Following characterization, both the cells and hydrogel were transplanted into the wound model, and the changes in wound healing pattern were analyzed.

Result: *In vitro* assays showed the biocompatibility and integrity of hydrogel which exhibited its potential for treatment approach. Histological and gene expression analysis exhibited enhanced healing in treated groups as compared to control.

Conclusion: Combining tissue engineered and cell based approaches in regenerative to address wound repair could be a better option to deal with most of the aspects of wound healing like hypoxia, excessive scarring, angiogenesis, and re-epithelization.

Keywords: Hydrogel, Hypoxic Wound, Mesenchymal Stem Cells, Regenerative Medicine, Tissue Engineering.

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