

Treatment of Lymphedema with Cell-Based Therapies: A Systematic Review
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Introduction

Lymphedema is a chronic condition that affects over 250 million people worldwide. It results from impaired lymphatic drainage, causing fluid and fat accumulation and eventually fibrosis of the affected limb. Lymphedema can be inherited (primary) or iatrogenic to surgery or parasitic infection (secondary). Breast cancer-related lymphedema is the most common etiology in the U.S. Current treatments have limited success and the disease mechanisms are not well understood. The purpose of this article is to review translational research into lymphedema therapies and its potential clinical impact.

Methods

A Pubmed search for novel treatment methods was performed with terms “lymphedema,” “cell therapy,” and “gene therapy.” Inclusion criteria were use of *in vivo* models, English language, and publication dates during the years 2000-2020.

Results

Secondary lymphedema is currently treated with compression garments and surgery; other approaches are being pursued. These include gene therapy (13 articles), stem cell transplant (16 articles), and immunosuppression (4 articles), which have all demonstrated considerable success in animal models of lymphedema. Growth factors such as VEGF-C are administered through adenoviral vectors and resolve limb swelling by inducing lymphangiogenesis. Stem cells derived from bone marrow or adipose tissue repair lymphatic damage directly by acquiring lymphatic characteristics or indirectly through paracrine signaling to surrounding cells. Immunosuppressive agents reduce inflammation and block antilymphangiogenic factors. Although these mechanisms have been studied in animals, only six human small studies were found, providing limited evidence.

Conclusion

Despite success in animal models, treatment in human subjects has been sparse. This limited translational feasibility is because of inadequate animal models, safety concerns, and lack of understanding about lymphedema pathophysiology. Although progress in lymphedema research has been made, further inquiry into its mechanism is needed in order to develop more effective and targeted therapies.