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Potential of Stem Cells Conditioned Medium (Secretome) Osteoarthritis Repair

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ABSTRACT:
Introduction: Osteoarthritis (OA) is a leading cause of disability, characterized by cartilage degeneration. Current therapies primarily alleviate symptoms rather than address cartilage damage. This systematic review evaluates the potential of mesenchymal stem cell (MSC) secretome as a regenerative treatment for OA. Method: A comprehensive literature search was conducted across EMBASE, Medline, Google Scholar and PLOS One databases using specific keywords related to MSCs and OA. Inclusion criteria focused on studies published from 2019 to 2024, while exclusion criteria eliminated reviews and non-experimental articles. The PRISMA guidelines were followed for screening and synthesis. Results: The review identified several studies demonstrating that MSC-derived secretome significantly improves clinical outcomes in OA. For instance, umbilical cord-derived MSC secretome showed enhanced cartilage repair and favorable biomarker changes with a favorable safety profile, indicating no adverse effects. Discussion: Findings suggest that MSC secretome offers a regenerative strategy targeting cartilage degeneration, contrasting with conventional therapies. The secretome's rich composition of bioactive molecules supports cartilage health and promotes tissue repair. However, variability in methodologies and limited sample sizes highlight the need for standardized protocols and larger randomized controlled trials. Conclusion: MSC secretome represents a promising therapeutic approach for OA, addressing the underlying pathology rather than merely alleviating symptoms. Continued research is essential to optimize treatment protocols and fully harness the potential of MSC secretome in improving OA management.

Keywords: Osteoarthritis, Secretome, MSCs, cartilage damage, cartilage healing

INTRODUCTION

Osteoarthritis (OA) is one of the leading causes of disability worldwide, especially in the elderly population. The disease is characterized by progressive degeneration of the cartilage joints, causing pain and loss of joint function. Although there are various therapies available,

there is no treatment that can reverse irreversible cartilage damage in OA. Conventional therapies for OA usually focus on symptomatic therapies, such as the use of analgesics and anti-inflammatory, as well as surgical intervention in severe cases. However, these therapies cannot fundamentally address cartilage damage, as they only aim to address the symptoms that occur. Therefore, a more innovative and regenerative therapeutic approach is needed to address OA. Enchymal stem cells (MSCs) have emerged as promising candidates for OA therapy due to their strong differentiation and immune regulatory capabilities. MSCs are obtained from various tissue sources, such as bone marrow, fatty tissue, placenta, and umbilical cord. In addition, MSCs can facilitate cartilage anabolism and extracellular matrix regulation through paracrine factors such as TGF-β, HGF, PGE2, PDGF, and IL-10.

Secretomes are a collection of bioactive molecules secreted by cells, including MSCs, which include exosomes and other paracrine factors. Secretome shows great potential in regenerative therapy. These components can repair cartilage damage by improving chondrogenic ability and reducing inflammation. Studies have shown that secretome MSCs can accelerate cartilage regeneration in animal models and in vitro.

This systematic review aims to conduct a comprehensive and transparent evaluation of the available evidence regarding the potential of secretome MSCs in OA therapy. This review will identify, select, and critically assess relevant studies to provide a summary of the current state of knowledge and identify gaps in the existing literature.

RESEARCH METHODS

The search was carried out using database from EMBASE, Medline and PLOS One using the keyword “(mesenchymal stem cells) OR (MSCs) OR (stem cell-conditioned medium) OR (secretome) AND (osteoarthritis) OR (OA)” After the search completed, the screening and synthesis process was carried out according to the PRISMA Guideline in making a Systematic Review.

RESULTS AND DISCUSSION

The systematic review presented herein highlights the emerging potential of mesenchymal stem cell (MSC) secretome as a promising therapeutic strategy for osteoarthritis (OA). The findings from the selected studies indicate that MSC-derived secretomes can significantly improve clinical outcomes in OA patients, suggesting a paradigm shift in how we approach the management of this debilitating condition. Unlike conventional therapies that primarily focus on symptom relief, the regenerative properties of MSC secretomes offer a more holistic approach that targets the underlying pathology of OA—cartilage degeneration.

One of the most compelling aspects of the studies reviewed is the consistent demonstration of MSC secretome's ability to enhance cartilage repair and regeneration15. For instance, the findings from Dilogo et al. and Partan et al. emphasize the secretome's role in promoting chondrogenic activity and improving biomarkers associated with cartilage health. This regenerative capability is attributed to the rich composition of bioactive molecules present in the secretome, such as growth factors and cytokines, which play critical roles in the modulation of inflammation and promotion of tissue repair. This highlights the need for further exploration into the specific components of the secretome that contribute to these beneficial effects, as understanding these mechanisms could lead to optimized therapeutic applications.

Additionally, the study by Damjanov et al provided valuable insights into the effectiveness of autologous conditioned serum (ACS) combined with triamcinolone injections for patients suffering from knee OA. This randomized controlled trial revealed that the use of ACS not only provided long-term pain relief but also significantly improved functional outcomes for patients, extending the short-term benefits typically associated with glucocorticoid treatments. This suggests that ACS may play a crucial role in enhancing the management of knee OA, offering patients sustained relief and improved quality of life.

Moreover, the long-term efficacy of MSC secretome, as observed in the studies, raises important considerations regarding dose, frequency, and route of administration. The study by Dilogo et al. noted that the maximum therapeutic effect was achieved six months post-injection, indicating that the timing of treatment may be crucial for maximizing benefits. This finding suggests that future research should focus on establishing standardized protocols for the administration of MSC secretome, which could enhance its clinical applicability and effectiveness in diverse patient populations.

The safety profile of MSC secretome treatments is another significant advantage that emerged from the reviewed studies. Both the open-label trials reported no adverse effects associated with the use of umbilical cord-derived secretome, which contrasts with some conventional OA treatments that carry risks of side effects. This finding is particularly relevant for elderly populations who are often at higher risk of complications from pharmacological interventions. The favorable safety profile of MSC secretome positions it as a viable alternative or adjunct to existing OA therapies, providing a new avenue for clinicians to consider in their treatment regimens.

Despite the promising results, several knowledge gaps and limitations warrant attention. The majority of the studies included in this review were open-label trials with limited sample sizes, which raises questions about the generalizability of the findings. Additionally, the lack of long-term follow-up data in some studies limits our understanding of the durability of the therapeutic effects. Future research should prioritize large-scale, multi-center randomized

controlled trials to validate the efficacy and safety of MSC secretome in OA treatment and to establish long-term outcomes.

Furthermore, the variability in the methodologies used across studies, such as differences in the source of MSCs and the specific techniques used for secretome extraction, presents challenges in drawing definitive conclusions. Standardization of these processes is essential to ensure reproducibility and comparability of results. Collaborative efforts among researchers and institutions could facilitate the development of unified protocols, thereby enhancing the robustness of future studies.

CONCLUSION

In conclusion, the findings of this systematic review underscore the potential of MSC secretome as a transformative therapeutic approach for osteoarthritis. By addressing the limitations of conventional therapies, MSC secretome offers a regenerative strategy that targets the fundamental issues associated with cartilage degeneration. As research in this field progresses, it is imperative to focus on elucidating the mechanisms of action, optimizing treatment protocols, and conducting rigorous clinical trials to fully realize the promise of MSC secretome in improving the quality of life for OA patients. The transition towards regenerative medicine represents a hopeful future for OA management, and continued exploration in this domain is essential for advancing therapeutic options.

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