REVIEW ARTICLE

CONTENTS

Role of stem cells in articular cartilage repair – a narrative review

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ABSTRACT

Articular cartilage injuries pose a major clinical obstacle due to their inability to regenerate contributed by cartilages' intrinsic properties and close association with osteoarthritis and progressive joint degeneration. Cartilage damage may be a consequence of acute trauma, repeated mechanical overload or age-related degenerative processes which often leads to chronic pain, joint dysfunction and a deterioration in the quality of life of patients.Established treatments such as; conservative management, intra-articular drug administrations and surgical cartilage repair typically provide relief. However, it's important to note that these treatments rarely lead to complete, permanent regeneration of natural hyaline cartilage. Recently, regenerative medicine has been paying significant attention to stem cell therapies. It aims to support cartilage repair while simultaneously impacting the intra-articular environment. It's safe to say that these approaches are increasingly being considered as potential therapeutic methods. Between the various cell populations, mesenchymal cells have gained particular attention due to their ability to promote chondrogenic differentiation, immunomodulatory properties, and paracrine effects.There is growing evidence suggesting that stem cells effects can be mediated not only by direct source replacement but are also contributed by the secretion of bioactive factors that influence physical processes, cartilage metabolism, and endogenous repair mechanisms. This narrative review aims to concisely summarize and critically evaluate novel evidence and scientific data on the biological repair mechanisms, clinical outcomes and safety assessment of stem cell-based therapies used to treat articular cartilage repair.

KEY WORDS: regenerative medicine, knee osteoarthritis, hyaline cartilage

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INTRODUCTION

Joint cartilage is a highly specialized connective tissue that supports the load-bearing system within synovial joints and enables resistance-free joint movement and efficient transfer [1]. The extracellular matrix of articular cartilage is characterized primarily by a high content of type II collagen and proteoglycans. This combination allows the joint cartilage to withstand significant mechanical loads without losing its ability to move smoothly within the joint. However, the low number of chondrocytes and the lack of blood vessels, nerves, and lymphatics significantly hinder the tissue's natural ability to heal itself after an injury [2]. As a result, cartilage defects, both focal and diffuse, tend to persist and may gradually worsen over time. These changes most often occur as a result of acute joint trauma, repeated mechanical overload or age-related degenerative processes. [1,3]. In the case of inability of effective biological repair, damaged cartilage may lead to deterioration of the joint surfaces, changes in subchondral bone and ultimately contribute to progression of osteoarthritis. This disease process is linked to chronic pain, impaired function, reduced quality of life and pose a major socioeconomic burden[3]. Over the past few decades, various surgical methods for cartilage repair have been developed in an attempt to restore the integrity of the joint surface. These methods include bone marrow stimulation treatments, osteochondral implants, and cell-based therapies such as autologous chondrocyte implantation.

Although these methods may provide better clinical outcomes in short and mid-term in some patients, long-term treatment outcomes are variable and the quality of the resulting regenerative tissue often does not provide optimum outcomes.Following injury, cartilage repair commonly results in the formation of fibrocartilage, which lacks the biomechanical properties and longevity

of native hyaline cartilage [1, 2, 4]. Consequently, conventional therapies frequently fail to achieve complete functional restoration. These limitations underscore the ongoing search for advanced regenerative strategies to improve cartilage repair. As a result, biological therapies are becoming a focus of interest and more spatialized than classical approaches, particularly ones based on modifying the intra-articular environment and promoting endogenous repair mechanisms. A rapidly emerging area of biomedical research, stem cell-based therapies show great promise for treatment. They are a promising approach for the treatment of many conditions because they provide distinct advantages over traditional methods due to their simultaneous trophic, immunomodulatory, and regenerative effects. Better understanding the biological basis and clinical potential of such therapies is key for their application in contemporary cartilage repair regimens.

AIM

This narrative review aims to critically evaluate and summarize the role of stem cells in promoting articular cartilage health post injury with particular emphasis on biological mechanisms of action, sources of stem cells, treatment outcomes and associated safety considerations published in articles between 2020 to 2025 [5].

MATERIALS AND METHODS

The current narrative review is based on analysis of peer-reviewed publications made between January 2020 and December 2025. Publications included in the review were randomized controlled trials, systematic reviews, meta-analyses and selected narrative reviews evaluating stem-cell-based therapies for cartilage repair and knee osteoarthritis[6]. Literature search was performed using major biomedical databases such as PubMed and reference lists of relevant articles were manually screened to confirm eligibility. Publications based on animal findings were excluded from the review. As the review is narrative in nature, no formal risk of bias was assessed.

REVIEW AND DISCUSSION

BIOLOGICAL MECHANISMS OF STEM CELL–MEDIATED CARTILAGE REPAIR

The contribution of mesenchymal stem cells (MSCs) in cartilage repair involves several related and interdependent mechanisms, directly by chondrogenic differentiation and indirectly through paracrine signaling [1,7]. Although in preliminary regenerative strategies, much emphasis was placed on the ability of MSCs to differentiate into a chondrocyte-like cell, novel studies help us understand that the main therapeutic effect of these cells is due to bioactive molecules secretions rather than direct structural replacement of tissue[8,9]. The secreted factors include cytokines, growth factors, and extracellular vesicles which collectively influence inflammatory processes, regulate cartilage metabolism and influence cell activity in the joint. In the osteoarthritic joint environment, paracrine signaling derived from mesenchymal stem cells exerts anti-inflammatory and immunomodulatory effects. This includes downregulating proinflammatory cytokine expression and promoting an anti-inflammatory macrophage phenotype [8].

Furthermore, MSCs may stimulate anabolic pathways within the cartilage and suppress catabolic processes associated with matrix degradation [9]. These mechanisms offer a commendable biological explanation for the common phenomenon of significant clinical improvement with not consistently structural cartilage regeneration which is demonstrated in imaging studies [10].

SOURCES OF MESENCHYMAL STEM CELLS AND THEIR CHONDROGENIC POTENTIAL

Mesenchymal stem cells can be isolated from various tissue sources, however, bone marrow and adipose tissue are the most common sources of mesenchymal stem cells in clinical practice [11]. Bone marrow derived mesenchymal stem cells demonstrate a high capacity for chondrogenic differentiation not only in vitro but also in vivo; however, the clinical use of these cells is limited due to the invasiveness of sampling procedures and relatively low cell yield [12]. On the contrary, adipose-derived stem cells and the stromal vascular fraction have practical advantages, including cell abundance, low donor-site morbidity and ease of access [13].

Recent clinical trials indicate that populations of adipose-derived cells carry the potential to produce similar efficacy in pain reduction and function as bone marrow derived MSCs for patients with cartilage defects and knee osteoarthritis [14,15]. Nevertheless, methods of administration, heterogeneous cell processing and dosing strategies make direct comparison of results across studies difficult and underscore the need to develop standardized treatment protocols.

CLINICAL OUTCOMES OF STEM CELL THERAPIES IN ARTICULAR CARTILAGE LESIONS AND KNEE OSTEOARTHRITIS

Numerous randomized controlled trials and meta-analyses have investigated the clinical efficacy of stem cell–

based therapies in individuals with knee osteoarthritis. In comparison with placebo, hyaluronic acid, or corticosteroid injections, interventions based on mesenchymal stem cells are consistently associated with clinically significant improvements in pain, functional outcomes, and patient-reported quality of life [16-19]. The positive outcomes were particularly noted in patients with early to moderate disease severity.

The evidence available for long-lasting regenerative capability of cartilage has been inconsistent. Studies have reported negative differences in MRI-derived images of cartilage thickness or composition (and therefore evidence of deterioration) whereas other studies were not able to demonstrate a consistent or definite change in cartilage structure [20,21]. These results highlight how cautious we need to be in interpreting results from imaging studies and that symptomatic improvement may not actually relate back to structural improvement at the cartilage level within the same patient. These results emphasize the importance of cautious and meticulous interpretations of imaging studies and suggest that symptomatic improvement may not correlate with the patient's macroscopic cartilage regeneration.

STEM CELLS COMBINED WITH BIOMATERIALS AND SCAFFOLD-BASED STRATEGIES

The integration of stem cells and biomaterials seeks to improve cell retention viability and incorporation into chondrocyte lesions. Scaffold-based and scaffold-free techniques have exhibited encouraging translational efficacy in preclinical and preliminary clinical investigations [22, 23]. These techniques may offer mechanical stabilization and targeted delivery of regenerative cells although high-level clinical data is scarce.

EMERGING CELL-FREE APPROACHES AND SAFETY CONSIDERATIONS

Novel cell-free methods such as exosomes derived from mesenchymal stem cells are advanced therapeutic options, which seem to preserve the positive paracrine effects of stem cells and evade the potential hazards of live stem cell transplantation [24]. Generally, stem-cell based therapeutic approaches have demonstrated favourable safety profiles in short and mid terms, and the adverse events are often mild and self-limited [25]. However, long-term safety, regulatory aspects and standardization of therapeutic procedures remain the main challenges for possible future clinical application [26].

CONCLUSIONS

Stem cell based therapies present a promising adjunctive treatment approach for the management of damaged articular cartilages as well as early-stage osteoarthritis. Indications of improvement with the therapy, based on published evidence from 2020 to 2025, show consistent positive outcomes for pain reduction as well as functional scores, whereas cartilage regeneration remains inconsistent. Further meticulously designed randomized controlled trials with long term follow up are required to determine and define the actual impact of stem cells on clinical routine practice.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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