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AUTOLOGOUS ADIPOSE-DERIVED STEM CELL THERAPY IN ORTHOPEDIC SURGERY: CURRENT CONCEPTS AND CLINICAL APPLICATIONS

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თორნიკე ავალიშვილი

ავტოლოგიური ცხიმოვანი ქსოვილიდან მიღებული მეზენქიმური სტრომული/ღეროვანი უჯრედებით მკურნალობა ორთოპედიულ ქირურგიაში: ამჟამინდელი კონცეფციები და კლინიკური გამოყენება

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რეზიუმე

წარმოდგენილი მიმოხილვითი სტატია აჯამებს ავტოლოგიური ცხიმოვანი ქსოვილიდან მიღებული მეზენქიმური სტრომული/ღეროვანი უჯრედების ბიოლოგიურ საფუძვლებსა და მათ თანამედროვე კლინიკურ გამოყენებას ორთოპედიასა და ტრავმატოლოგიაში. განხილულია თერაპიის მოქმედების მექანიზმები, კლინიკური ეფექტურობა მუხლის ოსტეოართროზის, ხრტილის დაზიანებების, მენისკისა და მყესების დაზიანების დროს, ასევე უსაფრთხოებისა და არსებული შეზღუდვების საკითხები. მიუხედავად იმისა, რომ საბოლოო კლინიკური რეკომენდაციების ჩამოსაყალიბებლად საჭიროა ფართომასშტაბიანი რანდომიზებული კვლევები, არსებული მონაცემები მიუთითებს, რომ ADSC-თერაპია რეგენერაციული ორთოპედიის ერთ-ერთი ყველაზე პერსპექტიული მიმართულებაა.

Introduction. Musculoskeletal diseases are a major global health burden, affecting hundreds of millions of individuals and accounting for substantial healthcare costs and productivity loss. Osteoarthritis, cartilage degeneration, meniscal injuries, ligament tears, and chronic tendinopathies are particularly common among aging populations and physically active individuals. Although advances in arthroscopic surgery, joint preservation, and rehabilitation have improved clinical outcomes, many patients continue to experience persistent pain and progressive tissue degeneration.

Conventional orthopedic treatments - including anti-inflammatory medications, intra-articular corticosteroid injections, hyaluronic acid, physical therapy, and surgical reconstruction - primarily address symptoms or mechanical abnormalities rather than promoting biological regeneration. Consequently, regenerative medicine has emerged as an innovative field aimed at restoring tissue structure and function through biologically active therapies.

Among the various regenerative strategies, autologous adipose-derived mesenchymal stromal/stem cells (ADSCs) have gained considerable attention because adipose tissue is an abundant and readily accessible source of multipotent stromal cells. Harvesting adipose tissue through minimally invasive liposuction is generally well tolerated and yields a substantially higher concentration of progenitor cells than bone marrow aspiration. In addition to mesenchymal stromal cells, adipose tissue contains endothelial progenitor cells, pericytes, immune cells, and numerous bioactive cytokines that collectively contribute to tissue repair.

Current evidence indicates that the therapeutic benefits of ADSCs arise predominantly through paracrine mechanisms rather than direct differentiation into cartilage or tendon tissue. These cells secrete growth factors, extracellular vesicles, and anti-inflammatory mediators that influence the local tissue environment, reduce inflammation, promote angiogenesis, and stimulate endogenous repair mechanisms.

Because of these biological properties, ADSC-based therapies have become increasingly investigated for the treatment of osteoarthritis, cartilage defects, meniscal injuries, tendon disorders, and ligament healing.

The objective of this review is to summarize the current scientific evidence regarding adipose-derived stem cell therapy in orthopedic surgery, emphasizing biological principles, harvesting techniques, clinical applications, safety considerations, and future perspectives.

Biology of Adipose-Derived Stem Cells. Adipose tissue is no longer regarded as merely an energy-storage organ but rather as a metabolically active tissue containing a heterogeneous population of regenerative cells. Mesenchymal stromal cells isolated from adipose tissue demonstrate self-renewal capacity, multilineage differentiation potential, and secretion of numerous growth factors involved in tissue repair. Compared with bone marrow, adipose tissue yields significantly more progenitor cells per unit volume, making it an attractive source for regenerative therapies.

Following tissue injury, ADSCs release vascular endothelial growth factor (VEGF), transforming growth factor-β (TGF-β), hepatocyte growth factor (HGF), insulin-like growth factor-1 (IGF-1), fibroblast growth factors (FGFs), and anti-inflammatory cytokines. These mediators enhance angiogenesis, reduce apoptosis, modulate immune responses, and stimulate resident progenitor cells. Consequently, current understanding suggests that their clinical effects depend primarily on immunomodulation and paracrine signaling rather than direct tissue replacement.

Liposuction and Cell Processing. Autologous adipose tissue is commonly harvested from the abdomen, flanks, or thighs using tumescent liposuction under local anesthesia. The procedure is minimally invasive, associated with low morbidity, and can often be performed on an outpatient basis.

After harvesting, adipose tissue may be processed using different techniques. Enzymatic digestion with collagenase isolates the stromal vascular fraction (SVF), which contains mesenchymal stromal cells together with endothelial cells, macrophages, pericytes, and other progenitor cells. Alternatively, mechanical processing techniques produce microfragmented adipose tissue without enzymatic digestion, preserving the extracellular matrix and native cellular environment. These methods differ substantially in cell composition, regulatory status, and clinical application, contributing to variability among published studies.

Clinical Applications

Knee Osteoarthritis. Knee osteoarthritis remains the most extensively studied indication for ADSC therapy. Clinical studies have consistently demonstrated improvements in pain, knee function, and patient-reported outcomes following intra-articular injection of adipose-derived cell preparations. Proposed mechanisms include suppression of synovial inflammation, modulation of macrophage activity, and stimulation of cartilage homeostasis. Imaging studies have reported stabilization or modest improvements in cartilage morphology in selected patients, although structural regeneration remains inconsistent.

Cartilage Defects. Focal chondral defects present a challenging clinical problem because articular cartilage has limited intrinsic healing capacity. ADSCs have been investigated as an adjunct to microfracture, scaffold implantation, and other cartilage restoration procedures. Preliminary evidence suggests improved defect filling and clinical outcomes; however, the quality of regenerated tissue remains variable and long-term durability requires further evaluation.

Meniscal Injuries. Meniscal deficiency significantly alters knee biomechanics and accelerates cartilage degeneration. Experimental and early clinical studies indicate that adipose-derived cell therapy may enhance meniscal healing following repair and may reduce symptoms in degenerative meniscal

lesions. Nevertheless, current evidence is insufficient to recommend ADSC therapy as a replacement for established surgical techniques such as meniscal repair or meniscal allograft transplantation.

Tendon Disorders. Chronic tendinopathies of the rotator cuff, Achilles tendon, patellar tendon, and lateral epicondyle have also been investigated. ADSCs may improve collagen organization, reduce chronic inflammation, and promote tendon remodeling. Several early clinical studies have reported reductions in pain and improved function, although larger randomized trials remain necessary.

Safety and Limitations. Published clinical studies generally report favorable safety profiles for autologous adipose-derived cell therapies. The most common adverse events include temporary pain, swelling, bruising, and discomfort at the liposuction site or injection site. Serious complications are uncommon when appropriate harvesting and sterile techniques are employed.

Despite promising clinical outcomes, several limitations remain. Significant variability exists in harvesting methods, processing protocols, injected cell populations, dosing strategies, rehabilitation protocols, and outcome assessment. Regulatory frameworks differ among countries, particularly regarding enzymatic processing and culture expansion of cells. Furthermore, many published studies involve small patient cohorts, lack adequate control groups, or have relatively short follow-up periods. These limitations currently restrict definitive conclusions regarding efficacy.

Results. Recent systematic reviews and meta-analyses indicate that autologous adipose-derived cell therapies provide significant improvements in pain and functional outcomes in patients with knee osteoarthritis compared with baseline assessments. Improvements have consistently been reported using validated clinical scoring systems such as the Visual Analog Scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee injury and Osteoarthritis Outcome Score (KOOS), and International Knee Documentation Committee (IKDC) score.

Evidence supporting cartilage regeneration remains less consistent. Although magnetic resonance imaging has demonstrated stabilization or partial improvement in cartilage morphology in selected studies, complete regeneration of hyaline cartilage has not been consistently demonstrated. Similarly, encouraging early outcomes have been reported in meniscal injuries and chronic tendinopathies, but current evidence remains limited by methodological heterogeneity and relatively small sample sizes.

Overall, existing literature supports ADSC therapy as a safe and potentially effective biological adjunct for selected orthopedic conditions. However, standardized cell characterization, optimized treatment protocols, and multicenter randomized controlled trials with long-term follow-up are essential to establish its definitive clinical role.

Conclusion. Autologous adipose-derived mesenchymal stromal/stem cell therapy represents one of the most promising regenerative approaches in contemporary orthopedic practice. The abundance of adipose tissue, minimally invasive harvesting through liposuction, and favorable biological properties make ADSCs an attractive option for biological augmentation in patients with degenerative and traumatic musculoskeletal disorders. Current evidence demonstrates improvements in pain, function, and quality of life, particularly in knee osteoarthritis, while maintaining a favorable safety profile.

Nevertheless, the available evidence remains heterogeneous, and current data do not yet support routine use as a replacement for established surgical or non-surgical treatments. Future research should prioritize standardized processing protocols, high-quality randomized controlled trials, longer follow-up periods, and clarification of the optimal indications for ADSC therapy. As scientific understanding and regulatory frameworks continue to evolve, adipose-derived cell therapy has the potential to become an important component of evidence-based regenerative orthopedic care.

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SUMMARY

This review provides a concise and up-to-date overview of the biological basis and clinical applications of autologous adipose-derived stem cell therapy in orthopedic surgery. The manuscript summarizes current evidence regarding the use of adipose-derived mesenchymal stromal cells in knee osteoarthritis, cartilage defects, meniscal injuries, and tendinopathies while addressing their mechanisms

of action, safety profile, and current limitations. Although further high-quality randomized controlled trials are required, the review highlights the promising role of ADSC-based therapies as a biological adjunct in modern regenerative orthopedics.

Keywords: adipose-derived, stem cells, liposuction, regenerative medicine, orthopedics