Sarem Journal of Medical Research. Volume 10, Issue 4, Winter 2025: 175- 177

The Role of Mesenchymal Stem Cells in the Treatment of Asherman's Syndrome and Endometriosis: Emerging Horizons in Reproductive Regenerative Medicine

ARTICLE INFO

DOI: 1052547/sjrm.10.4.1

Article Type

Editorial letter

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Abstract: Asherman's syndrome and endometriosis are two major and complex gynecologic disorders that have long drawn the attention of researchers and clinicians due to their profound implications for fertility, uterine function, and patients' quality of life [1,2]. In Asherman's syndrome, endometrial injury and the formation of intrauterine adhesions lead to severe disruption of the architecture and function of the basal endometrium, resulting in endometrial thinning, amenorrhea or oligomenorrhea, and infertility. Although hysteroscopic adhesiolysis remains the standard treatment and offers considerable benefits, it is often insufficient for restoring the regenerative capacity of the endometrium in patients with severe adhesions or extensive basal layer damage [3].

Keywords: Mesenchymal Stem Cells; Asherman Syndrome; Endometriosis; Reproductive Regenerative Medicine.

Received: 06 November 2025
Accepted: 06 December 2025
e Published: 10 December 2025

Article History

[DOI: DOI: 1052547/sjrm.10.4.1]

Editorial

Introduction

Asherman's syndrome and endometriosis are two major and complex gynecologic disorders that have long drawn the attention of researchers and clinicians due to their profound implications for fertility, uterine function, and patients' quality of life [1,2]. In Asherman's syndrome, endometrial injury and the formation of intrauterine adhesions lead to severe disruption of the architecture and function of the basal endometrium, resulting in endometrial thinning, amenorrhea or oligomenorrhea, and infertility. Although hysteroscopic adhesiolysis remains the standard treatment and offers considerable benefits, it is often insufficient for restoring the regenerative capacity of the endometrium in patients with severe adhesions or extensive basal layer damage [3]. On the other hand, endometriosis is characterized by a complex pathophysiology that involves chronic inflammation, dysregulated immune responses, epigenetic alterations, and the ectopic growth of endometrial-like tissue. Beyond causing severe pelvic pain and dysmenorrhea, the disease disrupts the pelvic microenvironment and compromises oocyte quality, ultimately diminishing fertility potential. Despite advances in hormonal therapies and surgical interventions over the past decades, challenges such as high recurrence rates, treatment-related adverse effects, and limited capacity to restore a physiologically normal pelvic milieu continue to hinder optimal management. The fact that current therapies are largely suppressive rather than restorative underscores the need for novel regenerative approaches [4].

In recent years, mesenchymal stem cells (MSCs) have emerged as a central focus of regenerative research in reproductive medicine owing to their unique capacities for differentiation, immunomodulation, paracrine signaling, and induction of neovascularization. These cells can be isolated from various sources, including bone marrow, adipose tissue, umbilical cord tissue, Wharton's jelly, and even menstrual blood, and their presence within injured tissues activates a cascade of molecular pathways that accelerate repair. Preclinical studies have demonstrated that MSCs, upon homing to damaged endometrial sites, secrete a range of trophic factors such as VEGF, IGF-1, HGF, and TGF-β3, which collectively promote angiogenesis, reduce fibrosis, and modulate macrophage activity, thereby suppressing chronic inflammation. Moreover, through strong paracrine effects, MSCs can activate resident endometrial stem cells, enhance cellular proliferation, and facilitate epithelial regeneration. In animal models of Asherman's syndrome, MSC transplantation has been associated with significant increases in endometrial thickness, improved stromal integrity, reduced collagen deposition, and enhanced pregnancy rates. These findings position MSCs as one of the most promising therapeutic candidates for refractory cases [5].

At the clinical level, early studies in patients with severe Asherman's syndrome have shown that intrauterine MSC infusion or the application of MSC-loaded biocompatible scaffolds can enhance endometrial regeneration. Several reports indicate improvements in menstrual patterns, increased endometrial thickness in subsequent cycles, and, in some cases, successful natural or assisted pregnancies. Although the number of available clinical trials remains limited, the emerging pattern of outcomes is encouraging and suggests that MSCs may offer a viable alternative for patients who do not benefit from conventional treatments. Concurrently, ongoing research on bioengineered scaffolds and MSC-laden smart hydrogels aims to improve cell survival, integration, and functional tissue regeneration, highlighting the growing integration of tissue engineering into uterine regenerative therapy [6].

In the context of endometriosis, the therapeutic potential of MSCs primarily stems from their immunoregulatory and anti-inflammatory properties. Animal models of endometriosis have shown that MSC administration can reduce the expression of proinflammatory cytokines such as TNF-α and IL-6, inhibit lesion progression, and alleviate associated pelvic pain. Furthermore, MSCs can shift macrophage polarization toward a reparative phenotype, thereby mitigating chronic inflammation and improving the pelvic microenvironment. In addition to these immunomodulatory functions, the antifibrotic effects of MSCs are of particular relevance, given that fibrosis and pelvic adhesions are integral components of endometriosis pathophysiology. Although these findings have not yet progressed to widespread clinical application, the future outlook indicates that MSC-based therapies may serve as valuable adjuncts to medical and surgical treatments and potentially reduce long-term recurrence rates [7].

Despite their substantial promise, several scientific and practical challenges must be addressed before MSCs can be widely integrated into routine clinical care. These include determining the optimal cell source, understanding functional differences among MSCs derived from various tissues, standardizing dosage, defining the ideal timing of administration relative to the menstrual cycle, and thoroughly evaluating potential risks such as unwanted differentiation, ectopic tissue formation, or aberrant angiogenesis. Critical considerations also extend to standardizing protocols for cell isolation, expansion, and storage, efforts that require the development of robust national and international guidelines. Furthermore, long-term safety monitoring is essential, particularly concerning potential risks such as tumorigenicity, infection, or epigenetic alterations.

[DOI: DOI: 1052547/sjrm.10.4.1]

Ethical and economic dimensions must also be incorporated into future clinical trial designs to ensure fair accessibility and responsible development of these emerging therapies.

Conclusion

In conclusion, MSC-based therapies offer a novel and compelling avenue for the management of challenging reproductive disorders such as Asherman's syndrome and endometriosis. By providing regenerative, immunomodulatory, and antifibrotic benefits that surpass the capabilities of conventional treatments, MSCs hold promise for transforming reproductive health care. Nevertheless, their successful translation into standardized clinical practice will require large-scale clinical trials, rigorous longitudinal safety studies, and close interdisciplinary collaboration among gynecologists, stem cell researchers, tissue engineers, and health-policy experts. Undoubtedly, the future of reproductive medicine is moving toward the integration of regenerative strategies, and MSCs have the potential to play a transformative role—provided their development proceeds on a foundation of robust evidence and stringent regulatory oversight.

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[DOI: DOI: 1052547/sjrm.10.4.1]