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Therapeutic Potential of Menstrual Blood Stem Cells in Reproductive Health Disorders: A Focus on POI and Endometriosis

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ABSTRACT

Reproductive health in women is maintained mainly by regulating hormones, immune strength and healthy tissues. Challenges such as chemotherapy-induced ovarian insufficiency and endometriosis disturb these systems, typically bringing about infertility and chronic pain. Conventional therapies ease the symptoms of a patient but do not address or repair the main problem that caused the disease. Using menstrual blood stem cells (MenSCs) in regenerative medicine is both safe, fair and does not require surgery. MenSCs can be easily recovered from menstrual fluid and have the same features as mesenchymal stem cells, including quick self-renewal, high proliferative activity, capabilities to differentiate into various cells and potent communication with other cells. Because of their capacity to regulate immune cells, encourage new blood vessels and aide in tissue healing, they are perfect for uses in reproduction. When chemotherapy leads to POI, MenSCs work to repair the ovaries and produce the necessary hormones due to their help in stopping cell death, promoting blood supply and stimulating the area. Since endometriosis is associated with immune and hormonal problems, herbal medicine might help by supporting these systems and reducing inflammation. Because MenSCs are not controversial, can be harvested more than once and fit a specific individual, they offer benefits over embryonic or surgically taken stem cells. This review points out the biological aspects, medical uses and potential of menstrual stem cells for treating reproductive problems in women. Advances have been made, but clinical studies should go on to set the rules for handling, multiplying and transplanting these cells and to assess possible risks in the long run. Nevertheless, MenSCs are a big advance in reproductive regenerative medicine and may transform both fertility treatment and the field of gynecology.

Keywords; menstrual blood-derived stem cells (MenSCs), Premature Ovarian Insufficiency (POI), hormone replacement therapy (HRT), natural killer (NK)

INTRODUCTION

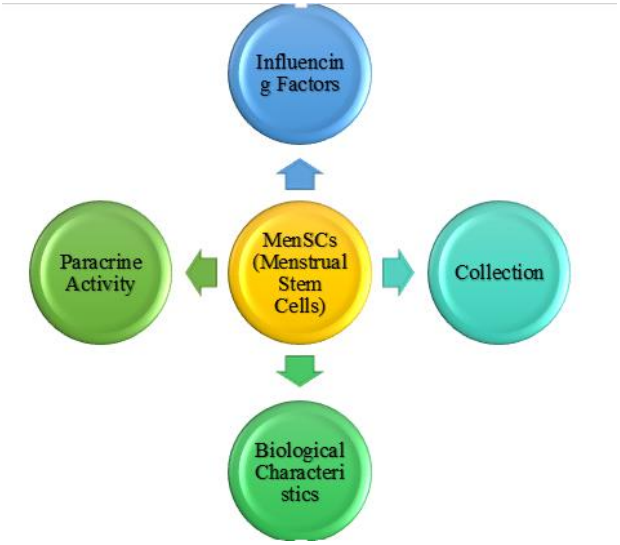
Reproductive health in women is guided by hormones, a well-functioning immune system and strong tissues. Medical therapies such as chemotherapy or conditions like endometriosis are sometimes responsible for infertility, failure of the ovaries and frequent pain. Traditional therapies help ease symptoms, but do not address the real damage or fix hormonal and immune system problems in the body. Menstrual blood-derived stem cells (MenSCs) have been introduced in recent times by regenerative medicine as a convenient, non-invasive and ethical source of mesenchymal stem cells. They are extracted during menstruation, making their process safe and ethical; embryonic stem cells, on the other hand, are collected by destroying human embryos and are very much debated. Each menstrual period which usually lasts 28 days, is regulated by hormones and can supply new stem cells.

Many people consider MenSCs to be better than the “gold standard” stem cell treatments which often require embryonic stem cells or surgery to harvest the cells. It is easy to obtain them and they create few ethical questions, as well as proliferating and differentiating very well. Besides numbers, their activity in the surrounding tissue and their immunological effects make them perfect for repairing tissues, managing the body’s overall immune reactions and restoring hormone levels in reproductive problems. This review studies the biological functions of MenSCs, their possible role in chemotherapy-damaged ovaries, endometriosis and how they are different from ethically controversial, as well as invasive sources of stem cells.

Menstrual Blood-Derived Stem Cells (MenSCs):

Menstrual blood-stem cells (MenSCs) are a unique and promising population of mesenchymal stem cells (MSCs) that you can easily harvest by using a non-invasive process. Whereas bone marrow and adipose tissue are hard to collect, MenSCs can be obtained

easily and repeatedly from menstrual fluid or endometrial tissue with no discomfort to the donor. Because collection is straightforward, MenSCs can be sampled again and again for regenerative treatments.



These cells display a unique biological profile, marked by their significant proliferative ability and multipotency, allowing them to differentiate into multiple cell types, including adipocytes, osteocytes, chondrocytes, as well as neurogenic and endothelial cells. Their expression of surface markers is consistent with typical MSCs, showing markers like CD73, CD90, and CD105, while lacking hematopoietic markers such as CD45 and CD34. A key feature is their strong paracrine activity—they release a wide range of cytokines, growth factors, and extracellular vesicles that facilitate tissue repair, encourage angiogenesis, and regulate immune responses. Despite these promising characteristics, various factors—including donor age, hormonal status, contraceptive use, and menstrual cycle phase—can affect their yield, biological function, and therapeutic efficacy. Exploring these factors is an ongoing research focus, critical for enhancing clinical applications.

MenSCs (Menstrual Stem Cells)

├── Collection

│ ├── Non-invasive

│ ├── From menstrual fluid/endometrial lining

│ └── Repeatable & donor-friendly

├── Biological Characteristics

│ ├── MSC markers: CD73, CD90, CD105

│ ├── Lack of hematopoietic markers (CD45, CD34)

│ ├── High proliferative capacity

│ └── Multipotency (can become: adipocytes, chondrocytes, osteocytes, neurogenic & endothelial cells)

├── Paracrine Activity

│ ├── Cytokines

│ ├── Growth factors

│ └── Extracellular vesicles

└── Influencing Factors

├── Donor age

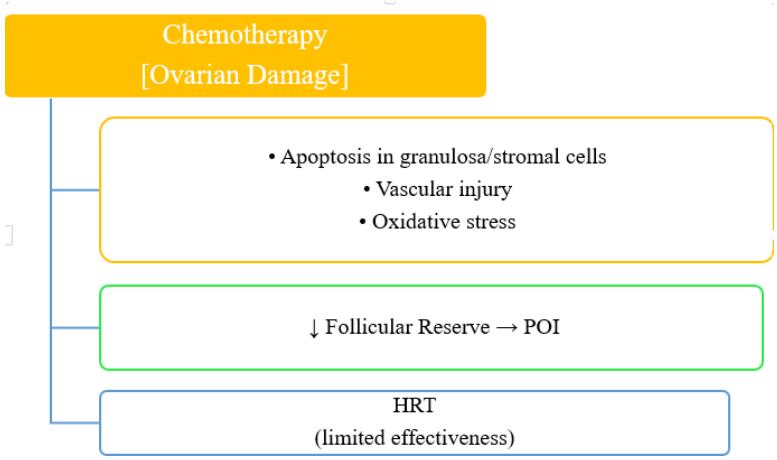
├── Menstrual cycle phase

├── Hormonal status

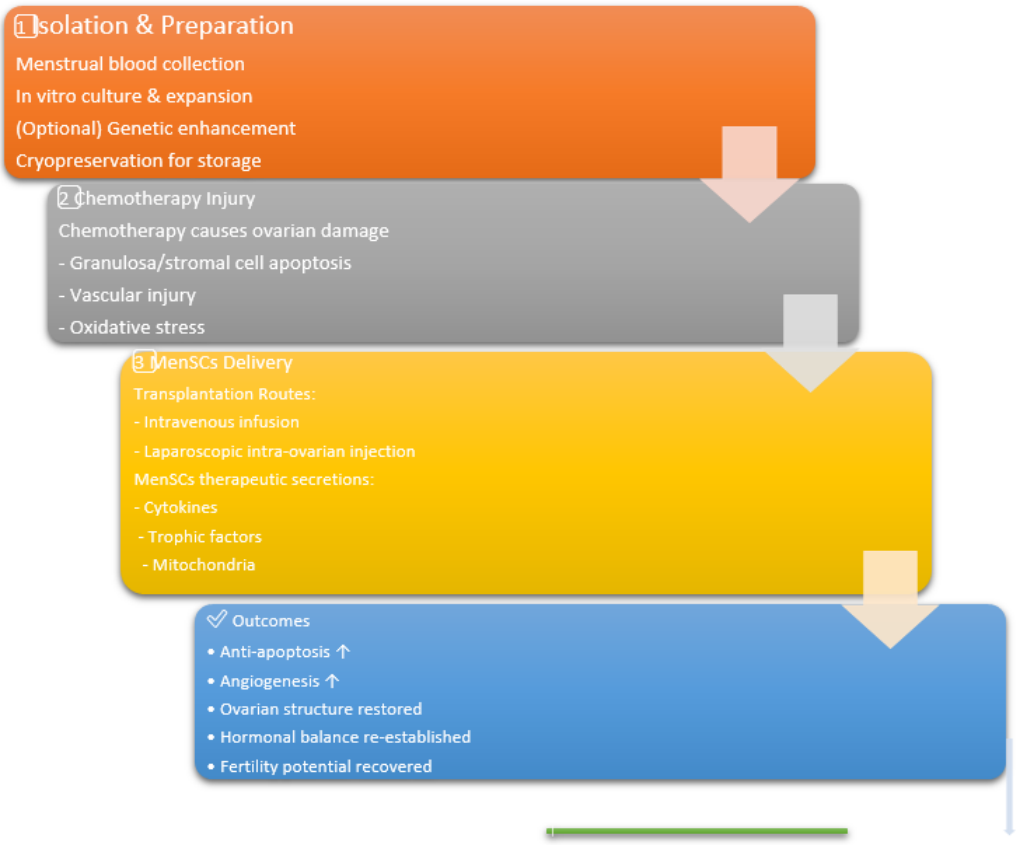
└── Contraceptive use

MenSCs in Chemotherapy-Induced Premature Ovarian Insufficiency (POI)

Chemotherapy plays a crucial role in cancer treatment but can unintentionally harm ovarian tissue due to its cytotoxic nature. Ovarian follicles, especially the primordial and growing ones, are extremely vulnerable to chemotherapeutic drugs, which trigger apoptosis in granulosa and stromal cells, impair blood vessels, and elevate oxidative stress levels. This sequence of events causes a notable decrease in follicular reserve, leading to premature ovarian insufficiency (POI), which is marked by hormonal imbalances, infertility, and overall health problems like osteoporosis and cardiovascular issues.



Traditional hormone replacement therapy (HRT) can alleviate some menopausal symptoms but does not prevent ongoing follicular depletion or restore reproductive capacity. In response to this challenge, researchers have investigated the regenerative potential of MenSCs. A three-stage autologous MenSC strategy has been proposed to repair ovarian damage caused by chemotherapy. The first stage involves isolating MenSCs from menstrual blood or endometrial tissue, culturing and expanding them in vitro, and potentially genetically modifying them to enhance their regenerative properties prior to cryopreservation. During the second stage, the ovarian tissue is subjected to chemotherapy, which induces cell apoptosis, vascular injury, and oxidative stress. In the final stage, MenSCs are delivered through methods such as intravenous infusion, laparoscopic intra-ovarian injection, or targeted arterial perfusion. Once introduced, MenSCs secrete cytokines, trophic factors, and mitochondria that promote anti-apoptotic signaling, stimulate angiogenesis, and facilitate tissue remodeling. These processes collectively aim to restore the structural integrity of the ovary, re-establish hormonal function, and potentially recover fertility, enabling the possibility of natural conception and improved reproductive outcomes.



Endometriosis: Pathogenesis and Underlying Mechanisms

The Pathology and Process by which Endometriosis Forms Endometriosis is a long-lasting gynecological problem where tissue similar to the lining of the uterus grows outside its cavity, primarily around the ovaries, in the peritoneum and in other pelvic organs. Conditions like immune dysfunction and hormone imbalance trigger a suitable situation for cancer tissues to maintain, expand and cause symptoms such as pain and difficulties with fertility.

Endometriosis

├── Key Feature

│ └── Endometrial-like tissue grows outside uterus

├── Immune Dysregulation

│ ├── IL-8, ENA-18 → Neutrophil/Macrophage Recruitment

│ ├── NK cell dysfunction (IL-8, TGF-β mediated)

│ ├── ↓ CD8+ T cells, ↑ CD4+ T cells

│ └── ↑ IL-10, IL-12 → Suppressed immune clearance

├── Hormonal Imbalance

│ ├── Progesterone resistance

│ ├── Aromatase (CYP19A1) overactivity → ↑ Estrogen

| └── Enhanced lesion survival & vascularization

└── Combined Effect

├── Immune escape + Estrogen-driven growth

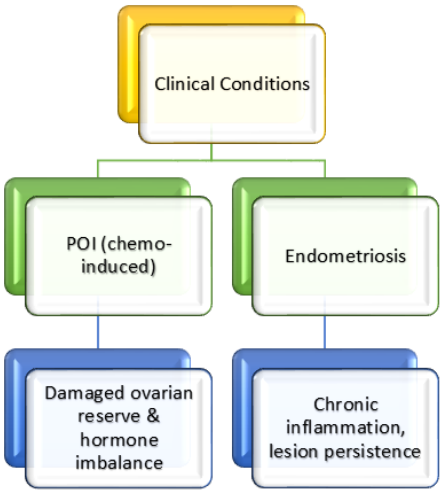
└── Persistent pain, infertility, inflammation

Immune Dysregulation: Immune Dysregulation: The immune system is important in causing and maintaining endometriosis. Such chemokines as IL-8, ENA-18 and HNPA-3 bring neutrophils and monocytes to places where they should not be which causes inflammation. In addition, natural killer (NK) cells, normally tasked with fighting off abnormal cells, have less ability to attack endometriotic cells because IL-8 and TGF-β prevent them from doing so. Changes can also be seen in dendritic cells and T lymphocytes such as an imbalance where there are low levels of CD8+ killer cells compared to CD4+ helper cells and this leads to immune responses being reduced by cytokines like IL-10 and IL-12. Because the immune system is suppressed, the abnormal tissue can implant, grow and continue to cause inflammation and discomfort.

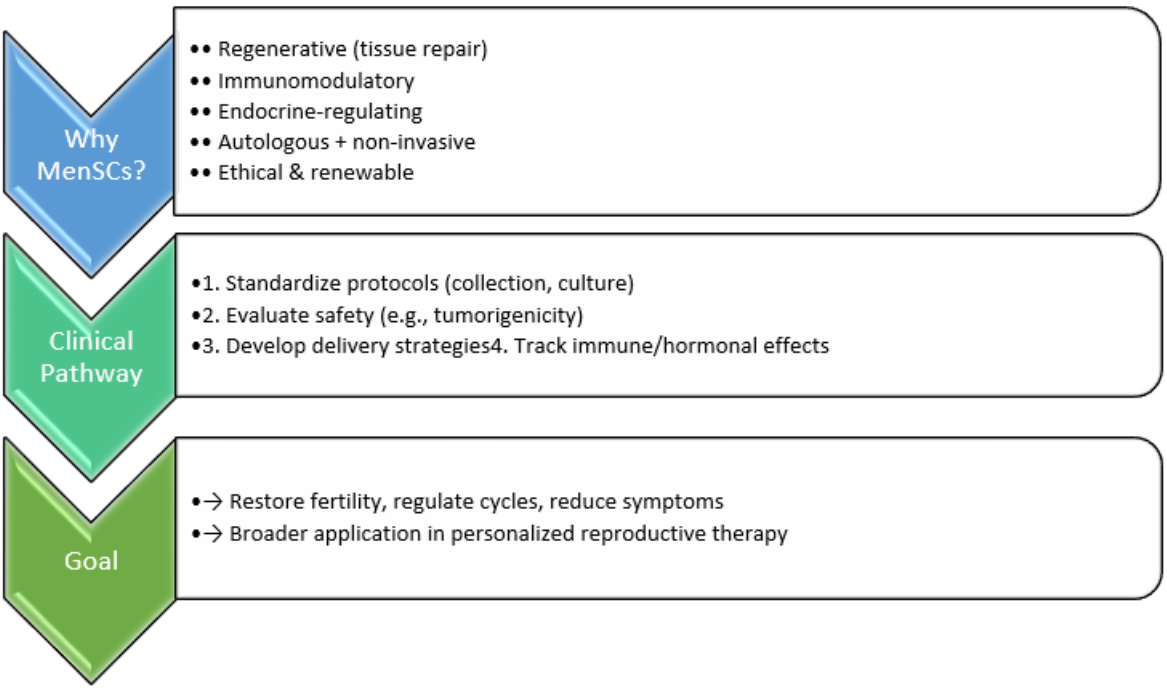
Hormonal Imbalance: Changes in hormone levels add to the chronic condition. Endometriosis is marked by the body not responding to progesterone as it should which impairs two vital processes: immune tolerance and the preparation of the endometrium for a pregnancy. Because of this, the endometrium becomes less able to accept an implanted embryo. At the same time, the aromatase enzyme (CYP19A1) becomes more active which results in extra local estrogen production and higher estrogen levels in the pelvic area. Increased estrogen levels in the body encourage growth of cells, blood vessels and inflammation around fibroids in the wrong locations which allows them to stay and develop further. Because of this environment, lesions continue to develop and can also lead to repeated pelvic pain, difficult menstruation and problems with reproduction.

Integrated Pathophysiology: Since these two systems are unbalanced, the cancer cells can evade the immune system and their hormones promote both their growth and the creation of new blood vessels. This makes it tough to choose a treatment, showing that the therapies should affect both the immune system and hormone levels of the patient at the same time.

Therapeutic Potential of MenSCs and Future Perspectives



Since immune problems, hormone changes and damage to tissues occur in chemotherapy-induced POI and endometriosis, using regenerative and immuno-related therapies is especially important. Since MenSCs can heal tissue, regulate the immune system and aide the endocrine system, they are extremely beneficial. Restoring fertility in women with POI could be possible by using their ability to repair chemotherapy-damaged ovaries. Also, since phytomedicines can fine-tune our immune function, they might be able to decrease lesions and the unpleasant symptoms linked with endometriosis. MenSCs are a good choice for personalized medicine because they are collected without insurance and used on the same person. Yet, to use these in clinical situations, more studies are required to set up standard protocols for isolating, growing and safely transplanting them into patients. Long-term testing such as evaluation for cancer risks, should be completed. It is important to look at how they respond to immune cells, find better ways to use them and discover their potential use in diagnosing and tracking reproductive issues.



.Conclusion

Using MenSCs as a source of stem cells is safe, ethical and offers good results in reproductive medicine therapy. Since their collection corresponds to the natural menstrual cycle that usually lasts 28 days and is governed by hormones, women can easily get renewable and gentle stem cells. Unlike embryonic stem cells which are debated because they are taken from embryos, MenSCs are collected freely from men, so they are ethically acceptable and can be used for a long time.

Due to their high production rate, ability to change into several cell types and immune-modulating function, these cells can support recovery of tissues in the ovaries damaged by chemotherapy, reestablish hormone activity and maybe help improve chances of getting pregnant. Also, since their effects on the immune and hormonal systems are known, they can offer alternatives for treating endometriosis. More research needs to be done to finalize procedures and confirm lasting safety, but MenSCs have made a big contribution to reproductive regenerative medicine because they are effective, safe and accepted by most. Using these cells might lead to better ways of treating fertility, helping women all over the world.

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