

Enhancing Endometrial Receptivity in Women with Thin Endometrium: Novel Approaches and Clinical Insights

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Abstract

Thin endometrium poses a significant challenge to women seeking pregnancy through assisted reproductive technologies (ART). The condition is characterized by insufficient endometrial thickness (≤ 7 mm), which impedes successful embryo implantation and lowers pregnancy success rates. This review explores current and emerging clinical strategies aimed at improving endometrial receptivity in women with thin endometrium[1]. By integrating pharmacological interventions, regenerative medicine, and advanced reproductive technologies, this article outlines an approach to enhance endometrial thickness, vascularization, and overall receptivity, ultimately improving ART outcomes[2].

Keywords: Thin endometrium, embryo implantation, reproductive medicine, regenerative therapies, assisted reproductive technology, platelet-rich plasma, stem cells, endometrial receptivity

1. Introduction

Endometrial receptivity is a crucial factor for successful embryo implantation and subsequent pregnancy during ART. An optimal endometrial thickness of ≥ 8 mm is widely considered necessary for implantation[3]. However, many women undergoing ART present with thin endometrium (≤ 7 mm), leading to challenges in achieving pregnancy. Factors such as intrauterine adhesions, chronic endometritis, hormonal imbalance, and idiopathic endometrial insufficiency can contribute to thin endometrium[4]. Traditional management strategies, including hormonal treatments, often show limited success, especially in refractory cases. Recent advances in regenerative medicine and individualized treatment approaches offer new hope for women with thin endometrium[5].

This review provides an overview of the current understanding of thin endometrium and outlines contemporary therapeutic approaches, including the integration of regenerative



medicine techniques to improve endometrial receptivity and increase the chances of a successful pregnancy.

2. Pathophysiology of Thin Endometrium

Thin endometrium results from various factors, both intrinsic and extrinsic to the individual. These include:

- **Iatrogenic causes:** Previous uterine surgeries such as curettage, myomectomy, or cesarean section can cause scarring and compromise endometrial growth.
- **Chronic infections:** Conditions like chronic endometritis can impair endometrial function.
- **Hormonal imbalances:** Low estrogen levels, which are often seen in women with polycystic ovary syndrome (PCOS) or after ovarian surgeries, can hinder endometrial development.
- **Idiopathic factors:** In some cases, the causes of thin endometrium remain unknown despite thorough evaluation.

At the molecular level, several factors contribute to the impaired endometrial development in women with thin endometrium:

- **Vascular endothelial growth factor (VEGF)** is essential for angiogenesis and blood vessel formation in the endometrium.
- **Leukemia inhibitory factor (LIF)** is required for the establishment of pregnancy, aiding in trophoblast invasion and endometrial receptivity.
- **Integrins** play a crucial role in embryo adhesion to the endometrial lining.

A lack of these critical factors leads to inadequate vascularization and poor endometrial development, thereby reducing the chances of successful embryo implantation.

3. Treatment Strategies for Thin Endometrium



Managing thin endometrium involves various therapeutic strategies, from pharmacological agents to advanced regenerative techniques.

3.1 Pharmacological Treatments

Estrogen Therapy is a cornerstone of treatment for thin endometrium. Estradiol, a synthetic form of estrogen, is commonly used to stimulate endometrial proliferation. However, this treatment alone may not be sufficient, especially in cases of refractory thin endometrium. Adjuncts such as **sildenafil citrate**, which improves uterine blood flow, and **pentoxifylline**, which enhances microcirculation, have been employed, but their efficacy varies.

3.2 Platelet-Rich Plasma (PRP) Therapy

PRP therapy involves the infusion of autologous platelet-rich plasma directly into the uterus. PRP contains a high concentration of growth factors such as **platelet-derived growth factor (PDGF)**, **transforming growth factor-beta (TGF- β)**, and **VEGF**, which stimulate angiogenesis, tissue repair, and cellular proliferation. Clinical studies have demonstrated that PRP can effectively increase endometrial thickness and improve pregnancy rates. PRP is especially beneficial in cases where conventional therapies have failed.

3.3 Stem Cell Therapy

Stem cell therapy is an emerging treatment for thin endometrium. **Bone marrow-derived stem cells (BMSCs)** and **menstrual blood-derived stem cells (MenSCs)** have shown promise in regenerating the endometrial lining. These stem cells release paracrine factors that enhance angiogenesis, epithelial regeneration, and immunomodulation. Early trials have shown promising results, although more robust clinical data is needed to establish stem cell therapy as a standard treatment.

3.4 Granulocyte Colony-Stimulating Factor (G-CSF)

G-CSF is a cytokine that stimulates the production and release of white blood cells. Recent studies suggest that G-CSF may also play a role in endometrial regeneration. By enhancing cellular proliferation and immune regulation, G-CSF can improve the quality of the endometrial lining and increase the likelihood of embryo implantation. Studies indicate that G-CSF administration, whether via intrauterine or subcutaneous routes, may improve both endometrial thickness and implantation success.

3.5 Hysteroscopic Evaluation and Treatment



In cases where structural issues contribute to thin endometrium (such as intrauterine adhesions), **hysteroscopic surgery** is a vital diagnostic and therapeutic tool. Adhesiolysis (removal of adhesions) and correction of other structural abnormalities, followed by hormone therapy, can enhance endometrial recovery and improve pregnancy outcomes.

4. Integrated Approach: Stepwise Protocol for Endometrial Receptivity

Based on the available evidence, we propose a stepwise, individualized treatment protocol to optimize endometrial receptivity:

Step	Intervention	Objective
1. Baseline Assessment	Transvaginal ultrasound, Doppler studies, hysteroscopy	Assess uterine anatomy, blood flow, and endometrial pathology
2. Initial Hormonal Therapy	High-dose estradiol, progesterone support	Promote endometrial growth and vascularization
3. Advanced Therapies	PRP infusion or G-CSF administration if hormonal therapy is ineffective	Stimulate endometrial regeneration and enhance receptivity
4. Stem Cell Therapy	Bone marrow-derived stem cells or MenSCs infusion (if refractory)	Improve angiogenesis and epithelial regeneration
5. Embryo Transfer Timing	ERA testing to personalize transfer timing	Optimize the timing of embryo transfer for better implantation

5. Discussion

The management of thin endometrium remains a complex challenge in reproductive medicine. While traditional estrogen therapy forms the basis of treatment, its success is often limited in cases of severe endometrial insufficiency. The integration of **platelet-rich plasma (PRP)**, **granulocyte colony-stimulating factor (G-CSF)**, and **stem cell therapies** provides



novel avenues for improving endometrial thickness and receptivity. These therapies offer significant potential, particularly in women who have failed conventional treatments.

Recent advancements in **personalized ART protocols**, such as **Endometrial Receptivity Analysis (ERA)**, enable clinicians to better synchronize embryo transfer with the optimal endometrial window, thereby improving implantation success. The combination of regenerative therapies with personalized ART strategies may revolutionize the treatment of thin endometrium, offering new hope for patients with previously poor prognosis.

6. Conclusion

Thin endometrium represents a major barrier to successful pregnancy in ART, but advances in pharmacological, regenerative, and surgical interventions offer promising solutions. A multidisciplinary approach, incorporating **PRP**, **G-CSF**, **stem cell therapy**, and **personalized treatment protocols**, can significantly enhance endometrial receptivity, improving pregnancy outcomes in women with thin endometrium. As research in this field continues, it is likely that these therapies will become a standard part of ART protocols, offering more women the possibility of successful pregnancy.

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