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Addressing Immunological Factors in Managing Thin Endometrium: A Clinical Approach to Enhance Fertility Outcomes

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Abstract

Thin endometrium, defined as an endometrial lining less than 7 mm in thickness, presents a significant barrier to successful pregnancy in women undergoing assisted reproductive technologies (ART)[1]. Immune system dysregulation, including autoimmune diseases and chronic inflammation, plays a critical role in reducing endometrial receptivity, making implantation difficult. This article explores the immunological aspects of thin endometrium, reviewing how immune factors, such as cytokines, autoantibodies, and altered immune cell function, contribute to poor implantation outcomes[2]. Furthermore, it proposes a clinical approach that integrates immunomodulatory therapies, including corticosteroids, intravenous immunoglobulin (IVIG), and mesenchymal stem cell therapy, to improve endometrial receptivity and ART success in women affected by immune-related endometrial dysfunction[3].

Keywords: Thin endometrium, immune system, autoimmune diseases, chronic inflammation, cytokines, ART, implantation, immunomodulation, fertility outcomes

1. Introduction

Endometrial thickness is a key determinant for successful embryo implantation and pregnancy in ART. A thin endometrium, typically ≤7 mm, is often associated with poor pregnancy outcomes. Among the various causes of thin endometrium, immune factors—particularly those related to autoimmune diseases, chronic inflammation, and immune system dysregulation—are increasingly recognized as significant contributors to endometrial dysfunction[4]. Autoimmune conditions such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and antiphospholipid syndrome (APS) are associated with altered immune responses that can impair endometrial receptivity, leading to implantation failure. This article provides an overview of immunological factors affecting endometrial

health and proposes an integrated approach to improving fertility outcomes through immune-modulating therapies[5].

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2. Pathophysiology of Immune System Dysregulation in Thin Endometrium

Immune system dysfunction in women with thin endometrium involves several key mechanisms:

- **Autoimmune Disorders and Cytokine Imbalance:** Autoimmune diseases, including SLE and RA, are characterized by the production of autoantibodies and immune cell activation that can lead to chronic inflammation. This inflammation negatively affects the endometrial lining, impairing the expression of key implantation markers such as integrins and leukemia inhibitory factor (LIF). Elevated levels of pro-inflammatory cytokines, such as TNF-α and interleukin-6 (IL-6), may further disrupt endometrial development and function, leading to reduced receptivity.
- **Impaired T-Cell Regulation:** In autoimmune diseases, dysregulated T-cell responses can alter the balance between pro-inflammatory and anti-inflammatory cytokines. This imbalance can impair the endometrial immune environment, which is crucial for both embryo implantation and maintenance of pregnancy. The presence of autoreactive T-cells in the uterus may also contribute to poor trophoblast invasion, further compromising implantation success.
- **Antiphospholipid Syndrome (APS):** APS is characterized by the presence of antiphospholipid antibodies, which are known to affect blood clotting and can lead to microvascular damage within the endometrium. This damage impairs blood flow to the uterine lining, preventing proper endometrial growth and reducing the likelihood of successful implantation.
- **Chronic Inflammation and Vascular Dysfunction:** Chronic inflammation associated with autoimmune diseases or other immune-related disorders leads to endothelial dysfunction, which is crucial for proper angiogenesis and uterine blood flow. Reduced blood flow to the endometrium further inhibits

endometrial regeneration and receptivity, contributing to thin endometrium and unsuccessful ART outcomes.

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3. Immunomodulatory Treatment Strategies

Given the immunological nature of thin endometrium in women with autoimmune or inflammatory conditions, immunomodulatory treatments can play a significant role in improving endometrial receptivity and fertility outcomes.

3.1 Corticosteroids

Corticosteroids, such as prednisolone, are commonly used to suppress immune responses in autoimmune diseases. In patients with thin endometrium, corticosteroids may reduce the inflammatory cytokine production that impairs endometrial growth. By modulating the immune system, corticosteroids help restore a more favorable endometrial environment for embryo implantation.

3.2 Intravenous Immunoglobulin (IVIG)

IVIG therapy involves the infusion of pooled immunoglobulins derived from human plasma. This treatment has been shown to suppress the production of pro-inflammatory cytokines and promote immune tolerance, improving implantation rates in women with autoimmune disorders or recurrent miscarriage. IVIG therapy may help balance the immune system and enhance endometrial receptivity by reducing the inflammatory milieu in the uterus.

3.3 Mesenchymal Stem Cell (MSC) Therapy

MSC therapy, derived from sources such as bone marrow or adipose tissue, has shown promise in promoting tissue regeneration and reducing inflammation. MSCs secrete paracrine factors that support angiogenesis, epithelial regeneration, and immunomodulation. In women with autoimmune diseases, MSC therapy may improve endometrial regeneration, increase vascularity, and enhance the overall receptivity of the endometrium, thus improving ART outcomes.

3.4 Low Molecular Weight Heparin (LMWH)

In patients with antiphospholipid syndrome, LMWH can be used to prevent blood clot formation and improve uterine blood flow. By enhancing microcirculation, LMWH can

promote endometrial growth and improve the chances of implantation in women with APS-related thin endometrium.

3.5 Personalized ART Protocols

In women with immune-related thin endometrium, personalized ART protocols are essential. These protocols should include immune system monitoring, cytokine profiling, and personalized embryo transfer timing based on the patient's immune status. For example, the Endometrial Receptivity Array (ERA) test can be used to identify the optimal window for embryo implantation, thus enhancing pregnancy rates in women with compromised endometrial environments.

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4. Case Presentation

Patient Information:

- **Age:** 34
- **Diagnosis:** Systemic Lupus Erythematosus (SLE) with antiphospholipid syndrome (APS)
- **Clinical History:** The patient presented with a history of recurrent miscarriage and failed ART attempts. Transvaginal ultrasound revealed thin endometrium (≤6 mm) during multiple ART cycles. Blood tests confirmed the presence of antiphospholipid antibodies, and her lupus condition was well-controlled with hydroxychloroquine.

Clinical Approach:
The patient underwent a combination of immunomodulatory treatments, including corticosteroid therapy (prednisolone 10 mg/day), IVIG infusions (2 g/kg), and LMWH for thrombosis prevention. Additionally, MSC therapy was administered to enhance endometrial regeneration. After these treatments, the patient’s endometrial thickness improved to 8 mm, and her uterine blood flow normalized.

Outcome:
Embryo transfer was performed based on the ERA test, which identified the optimal implantation window. The patient successfully achieved a clinical pregnancy, confirmed by ultrasound at 6 weeks, with a subsequent healthy pregnancy and delivery.

5. Discussion

Immunological factors, including autoimmune diseases and chronic inflammation, significantly contribute to thin endometrium and impaired implantation in ART. Dysregulated immune responses alter endometrial function by disrupting angiogenesis, impairing immune tolerance, and causing chronic inflammation. By integrating immunomodulatory therapies such as corticosteroids, IVIG, MSC therapy, and LMWH, clinicians can address the underlying immune dysfunction and improve the chances of a successful pregnancy. Personalized ART protocols based on immune status and endometrial profiling further optimize outcomes, providing new hope for women with immune-related endometrial dysfunction.

6. Conclusion

Addressing the immunological aspects of thin endometrium is crucial for improving ART outcomes in women with autoimmune disorders, chronic inflammation, and immune system dysregulation. An integrative, multidisciplinary approach combining conventional and emerging therapies offers a promising solution to enhance endometrial receptivity and increase pregnancy rates. Future research into the immunological mechanisms underlying thin endometrium will provide valuable insights into optimizing treatment protocols for these patients.

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