Perspective
iMedPub Journals
www.imedpub.com

Reproductive Immunology: Open Access
ISSN 2476-1974

2025
Vol.9 No.1:05

Immunomodulatory Therapies for Recurrent Miscarriage: Current Perspectives

Louise Jaro*

Department of Gynecology and Obstetrics, University Hospital of Fribourg, 1708 Fribourg, Switzerland

***Corresponding author:** Louise Jaro, Department of Gynecology and Obstetrics, University Hospital of Fribourg, 1708 Fribourg, Switzerland, E-mail: Jaro.louis@h-fr.ch

Received date: February 01, 2025, Manuscript No. iprioa-25-20428; **Editor assigned date:** February 03, 2025, PreQC No. iprioa-25-20428 (PQ); **Reviewed date:** February 15, 2025, QC No. iprioa-25-20428; **Revised date:** February 22, 2025, Manuscript No. iprioa-25-20428 (R); **Published date:** February 28, 2025, Doi: 10.21767/2476-1974.9.01.05

Citation: Jaro L (2025) Immunomodulatory Therapies for Recurrent Miscarriage: Current Perspectives. Reproductive Immunol Open Acc Vol.9 No.1:05

Introduction

Recurrent Miscarriage (RM), defined as two or more consecutive pregnancy losses before 20 weeks of gestation, affects approximately 1–2% of women of reproductive age. While genetic, anatomical, endocrine and thrombophilic causes are well established, immunological factors are increasingly recognized as a significant contributor to recurrent pregnancy loss. Pregnancy represents a unique immunological state in which the maternal immune system must tolerate the semi-allogenic fetus while maintaining defense against infections. Dysregulation of this delicate balance, including aberrant function of Natural Killer (NK) cells, T lymphocytes, cytokine profiles and autoantibodies, can disrupt implantation and early placental development, leading to miscarriage. Immunomodulatory therapies aim to restore this balance, enhance maternal-fetal tolerance and improve pregnancy outcomes. Despite growing interest, their application remains complex, with varying degrees of clinical efficacy. This article explores the current perspectives on immunomodulatory strategies for RM, including their mechanisms, evidence base and clinical considerations [1].

Description

The immunological basis of recurrent miscarriage is multifactorial. Aberrant NK cell activity, including excessive cytotoxicity and altered expression of activating and inhibitory receptors, can impair trophoblast invasion and spiral artery remodeling. Dysregulation of T cell subsets, particularly a deficiency in regulatory T cells (Tregs) and a skewing toward Th1 or Th17 pro-inflammatory responses, can further disrupt maternal-fetal tolerance. Additionally, elevated pro-inflammatory cytokines such as Tumor Necrosis Factor-Alpha (TNF-α) and InterFeron-Gamma (IFN-γ), along with the presence of autoantibodies especially antiphospholipid antibodies create an environment hostile to implantation and early embryonic development. Understanding these immunological mechanisms has paved the way for therapeutic interventions aimed at modulating immune responses to support pregnancy. One of the most widely studied immunomodulatory approaches is the use of corticosteroids. Low-dose corticosteroids, such as prednisolone, exert anti-inflammatory effects by reducing cytokine production, suppressing NK cell activity and enhancing Treg function. In women with RM associated with elevated NK cell activity or autoimmune disorders, corticosteroids may improve implantation and early pregnancy maintenance. However, clinical trials have yielded mixed results and long-term use carries potential risks, including maternal hypertension, glucose intolerance and fetal growth restriction. Therefore, careful patient selection and monitoring are essential when considering corticosteroid therapy [2].

Intravenous ImmunoGlobulin (IVIG) therapy is another immunomodulatory strategy employed in RM. IVIG is thought to modulate the maternal immune response by neutralizing pathogenic autoantibodies, inhibiting NK cell cytotoxicity and promoting Treg expansion. Several clinical studies have investigated IVIG in women with RM, particularly those with elevated NK cell activity or autoimmune disorders. While some trials have demonstrated improved live birth rates, others have reported limited benefit and meta-analyses remain inconclusive. The high cost, intravenous administration and potential side effects including infusion reactions and transient renal or hepatic alterations limit its routine use [1].

Heparin and low-dose aspirin, although primarily anticoagulant agents, also possess immunomodulatory properties. In women with antiphospholipid syndrome (APS), these agents prevent thrombosis and complement activation at the maternal-fetal interface, reducing pregnancy loss. Heparin may additionally modulate cytokine expression and NK cell activity, contributing to its beneficial effects. Combined therapy with aspirin and heparin is now considered standard of care for women with APS-related RM, resulting in significant improvement in live birth rates.

Emerging therapies targeting specific immune pathways offer promise for more precise interventions. Tumor necrosis factor-alpha inhibitors, such as etanercept or infliximab, have been investigated in experimental models and small clinical studies for women with RM associated with elevated TNF-α. These biologics may reduce inflammation, enhance trophoblast survival and promote maternal-fetal tolerance. Similarly, therapies aimed at augmenting Treg populations, such as adoptive Treg transfer or low-dose interleukin-2 therapy, are under exploration, with the goal of restoring immune tolerance without broad immunosuppression. These approaches remain largely experimental and require rigorous evaluation before routine clinical implementation [2].

Conclusion

Immunomodulatory therapies represent a promising avenue for managing recurrent miscarriage, particularly in cases associated with immunological dysregulation. Strategies such as corticosteroids, intravenous immunoglobulin and heparin combined with aspirin target specific immune mechanisms, including NK cell activity, cytokine imbalances and autoantibody-mediated injury, to enhance maternal-fetal tolerance and improve pregnancy outcomes. Emerging biologics and cellular therapies offer potential for more targeted interventions, although clinical evidence remains limited.

Personalized treatment guided by detailed immune profiling, coupled with supportive lifestyle interventions and reproductive technologies, provides the most comprehensive approach to addressing RM. Ongoing research and well-designed clinical trials are crucial to refining these therapies, improving efficacy and ensuring safety. Understanding the immunological underpinnings of recurrent miscarriage not only informs therapeutic strategies but also offers insights into the broader mechanisms governing maternal-fetal tolerance and reproductive success.

Acknowledgement

None.

Conflict of Interest

None.

References

1. Coulam CB, Roussev RG (2002) Role of T Cell activation and inhibition markers in diagnosing women experiencing immunologic implantation failure after in vitro fertilization and embryo transfer. Am J Reprod Immunol 48: 138-138.
2. Daya S and Joanne G (1994) The Effectiveness of Allogeneic Leukocyte Immunization in Unexplained Primary Recurrent Spontaneous Abortion. Am J Reprod Immunol 32: 294-302.