



# Recurrent Implantation Failure and Innovative Therapeutic Options: A Systematic Review

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## ABSTRACT

**Introduction:** Recurrent implantation failure (RIF) is a clinical phenomenon defined as failure to become pregnant after the transfer of at least three good-quality embryos in three cycles in women under 40 years of age. The causes for couples with RIF can be anatomical abnormalities, aneuploidy, male factors, immunology, thrombophilia, impaired endometrial receptivity, and microbiome. Impaired endometrial receptivity is estimated to account for two-thirds of implantation failures. Studies have focused on improving endometrial receptivity for success rates in patients with RIF. This systematic study aimed to evaluate novel treatment options for RIF.

**Search Strategy:** The Key findings were identified by searching the PubMed, Scopus, and Web of Science databases. The terms "innovative treatment options and recurrent implant failure" were searched, and 30 papers were reviewed.

**Results:** According to the studies examined, various methods were used to regenerate and improve the thickness of the endometrium, including the use of growth hormone, letrozole, medroxyprogesterone acetate, granulocyte colony-stimulating factor, platelet-rich plasma (PRP), lymphocytes immunotherapy, and endometrial scratch. In addition to these methods, new promising treatment options emerged for RIF, particularly in resistant endometrium situations, including endometrial mesenchymal stem cells and their mixture with PRP. Research suggested that stem cell therapy could enhance endometrial receptivity by promoting angiogenesis and modulating the immune response. The other innovative regenerative therapy for RIF cases included the use of exosomes. These vesicles carry various bioactive molecules that can regulate gene expression and signaling pathways in recipient cells. They could also modulate the crosstalk between the embryo and the endometrium, affecting endometrial receptivity, immune response, and angiogenesis, which are critical for successful implantation.

**Conclusion and Discussion:** While the innovative options show potential in addressing resistant endometrium and improving outcomes in RIF patients, they are still considered experimental approaches. Further research is necessary to confirm their clinical utility. However, more research is also needed to establish the safety and efficacy of these cell-based therapies.

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