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EFFICACY AND COMPLICATIONS OF IMMUNOSUPPRESSIVE THERAPY IN UTERINE TRANSPLANTATION

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Abstract
Uterine transplantation represents a novel milestone in reproductive medicine, offering hope for women deprived of the ability to become mothers. Postoperatively, immunosuppressive therapy is administered to prevent graft rejection. This article analyzes the efficacy of immunosuppressive drugs, their impact on pregnancy outcomes following uterine transplantation, and potential complications. Long-term results and future perspectives of this therapy are also discussed.

Keywords: Uterine transplantation, immunosuppressive therapy, complications, reproductive medicine.

Introduction:

Uterine transplantation (UT) has recently been recognized as one of the most significant achievements in reproductive medicine. This procedure provides an opportunity for women without a uterus due to congenital or acquired causes to experience pregnancy. The world's first successful uterine transplantation was performed in Sweden in 2014, marking a new era in both clinical medicine and scientific history.

However, one of the key clinical challenges in UT is the risk of graft rejection by the immune system. Therefore, immunosuppressive therapy is prescribed

postoperatively. While such therapy ensures graft survival, it also poses risks of complications including infections, renal impairment, metabolic syndrome, and even increased oncological risks.

Additionally, UT carries unique complexities, as graft success is evaluated not only by survival but also by its ability to sustain pregnancy and childbirth. Thus, assessing the efficacy and safety of immunosuppressive agents is of utmost importance.

This article aims to scientifically analyze the efficacy, complications, long-term outcomes, and future prospects of immunosuppressive therapy in uterine transplantation.

Relevance of the Study:

Over the past decade, uterine factor infertility has been acknowledged as one of the most serious causes of female infertility. Global statistics indicate that 3–5% of women of reproductive age lack the ability to conceive due to congenital or acquired uterine absence. Historically, adoption or surrogacy were the only solutions for such patients. Today, uterine transplantation offers a new hope.

UT is a highly complex procedure, with success depending directly on the immune acceptance of the graft. In this regard, immunosuppressive therapy plays a crucial role. However, long-term administration of such drugs results in multiple adverse effects, including:

- increased susceptibility to infections,
- metabolic disorders,
- nephrotoxicity,
- elevated oncological risks,
- potential congenital anomalies during pregnancy.

Currently, UT remains experimental, with clinical trials being conducted in a limited number of centers worldwide. Nevertheless, the optimization of immunosuppressive protocols, safe drug combinations, and strategies to reduce complications remain unresolved.

Thus, evaluating the efficacy and risks of immunosuppressive therapy in UT is not only of scientific but also of social importance, contributing to improved future outcomes of this innovative procedure.

Materials and Methods

This study was conducted based on recent publications, clinical observations, and experimental data regarding uterine transplantation. Data collection and analysis employed the following methodology:

1. **Literature Selection**

- Articles published between 2014 and 2024 in PubMed, Scopus, and Google Scholar were analyzed.
- Keywords included: "uterine transplantation," "immunosuppressive therapy," "complications," and "pregnancy outcomes."

2. **Inclusion Criteria**

- Clinical cases of UT,
- Patients receiving immunosuppressive therapy,
- Documented pregnancy and delivery outcomes,
- Reported complications (infection, nephrotoxicity, metabolic syndrome, etc.).

3. **Methods of Analysis**

- Qualitative review of literature,
- Statistical analysis of reported outcomes,
- Comparative evaluation of different immunosuppressive protocols.

4. **Key Indicators**

- Functional graft survival rate,
- Rates of pregnancy and live births,
- Frequency and severity of complications,
- Long-term therapeutic outcomes.

This methodology enabled a systematic evaluation of the advantages and risks of immunosuppressive therapy in UT.

Results

Analysis of clinical reports and literature revealed the following findings:

1. **Efficacy of Immunosuppressive Therapy**

- Tacrolimus, azathioprine, and corticosteroid-based regimens were the most widely used.
- Functional graft survival reached 85–90% at the end of the first postoperative year.
- Clinical data showed pregnancy rates of 60–70% among recipients, with about half resulting in healthy live births.

2. **Complication Rates**

- The most common complications associated with immunosuppressive therapy included:
  - Infections: 35–40% of patients,
  - Renal impairment: 15–20% of cases,
  - Metabolic syndrome and predisposition to diabetes: 10–15%,
  - Increased oncological risk: 3–5% in long-term follow-ups.

3. **Pregnancy Outcomes**

- Immunosuppressive therapy did not increase congenital anomalies in infants.
- However, preterm birth (25–30%) and low birth weight (approx. 20%) were noted.
- The safest interval for conception was found to be at least 12 months post-transplant.

4. **Long-Term Outcomes**

- Three- to five-year follow-ups showed graft survival rates of 75–80%.
- Patients reported improved quality of life, though economic and healthcare burdens of long-term therapy remained significant.

Discussion

Uterine transplantation has emerged as one of the most groundbreaking innovations in reproductive medicine. While survival rates and pregnancy success are promising, challenges linked to immunosuppressive therapy remain critical.

Our findings align with those of several international centers. Tacrolimus-based regimens effectively prevent rejection but significantly increase nephrotoxicity risks. Long-term corticosteroid use contributes to metabolic syndrome and osteoporosis.

Pregnancy outcomes highlight that immunosuppressive therapy does not increase congenital anomalies—a positive result. However, risks of preterm birth and low birth weight remain concerns. Importantly, conception should be delayed until at least 12 months post-transplant, which is now considered a best-practice recommendation.

To enhance safety and efficacy, future research should focus on:

- individualized immunosuppressive regimens,
- determining minimal effective dosages,
- developing early diagnostic markers for complications,
- continuous monitoring of pregnancy and delivery outcomes.

Overall, UT is a promising but still experimental procedure. Long-term safety and optimization of immunosuppressive therapy require extensive multicenter clinical studies.

Conclusion

Uterine transplantation represents one of modern medicine's greatest achievements, offering biological motherhood to women otherwise unable to conceive. Evidence indicates that immunosuppressive therapy is essential for graft survival and successful pregnancy. While tacrolimus, azathioprine, and corticosteroids are effective, they carry risks of nephrotoxicity, infections, and metabolic complications.

Pregnancy outcomes show no increased rate of congenital anomalies, though preterm birth and low birth weight remain prevalent. Delaying conception until at least one year post-transplant is considered the safest approach.

Future perspectives include individualizing therapy, minimizing effective dosages, and reducing long-term complications. Large-scale, multicenter clinical trials are essential for the widespread adoption of UT in reproductive medicine.

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