Research Protocol

Hysteroscopy for Termination of Early Pregnancy Complicated with Intrauterine Adhesions: A Prospective Observational Study

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1. Research Background

Intrauterine adhesion (IUA), also known as Asherman's syndrome, refers to a series of syndromes characterized by partial or complete uterine cavity occlusion caused by damage to the endometrial basal layer from various factors. Its primary clinical manifestations include hypomenorrhea, recurrent spontaneous abortion, and infertility. Uterine cavity surgical operations constitute the predominant etiology, with a high incidence of IUA following induced abortion; the risk of IUA rises in tandem with the number of curettage procedures.Hysteroscopic adhesiolysis represents the primary treatment for IUA at present, yet its postoperative recurrence rate remains substantial, with higher recurrence observed in patients with severe adhesions. IUA has become a major disease impairing reproductive health among women of childbearing age. For patients with fertility demands, those with severe adhesions often require repeated adhesiolysis, which brings severe surgical trauma, high medical costs, and unsatisfactory prognosis, severely compromising women's physical and mental well-being.

According to the *2021 China Health Statistics Yearbook* released by the National Health Commission, the number of induced abortions (including medical abortion, vacuum aspiration, forceps curettage, and second-trimester induction) in China has been on the rise since 2009, reaching 8.962 million cases in 2020. The induced abortion rate climbed from 26.8% in 2009 to 61.0% in 2020, featuring prominent characteristics including high total volume, young patient age, high proportion of unmarried and nulliparous women, and high repeated abortion rates. When terminating pregnancy in patients with early pregnancy combined with IUA, structural uterine cavity distortion and gestational sac occlusion by adhesion bands frequently lead to incomplete abortion with retained gestational tissue, failed abortion, or uterine perforation, often necessitating reoperation and exacerbating surgical trauma, financial burden and psychological distress for patients. Meanwhile, many patients with IUA retain future fertility demands and require concurrent management of adhesions.

Hysteroscopy enables direct visualization to remove intrauterine gestational tissue, lowering risks of residual tissue and reoperation while simultaneously addressing existing intrauterine adhesions. Postoperative anti-adhesion interventions can restore uterine cavity anatomy and endometrial function, improve subsequent fertility, reduce psychological burden, and cut down time and economic costs associated with subsequent rehospitalization for adhesiolysis.

2. Research Objectives

1. To investigate the clinical outcomes and advantages of concurrent hysteroscopic pregnancy termination and adhesiolysis in patients with early pregnancy combined with IUA via clinical controlled research, and provide reliable clinical evidence for whether simultaneous hysteroscopic management of IUA should be performed during induced abortion for this patient population.
2. To analyze the impacts of immune cell subsets, inflammatory mediators, vascular remodeling markers detected via immunohistochemistry of decidual tissue on disease progression, so as to offer references for clinical management and treatment of this condition.

3. Research Design and Content

This is a prospective controlled study. Patients admitted to the Family Planning Ward of our hospital for termination of early pregnancy complicated with IUA will be enrolled after ethical approval, screened per predefined inclusion and exclusion criteria.

- **Experimental Group**: Patients receiving hysteroscopic abortion combined with concurrent intrauterine adhesiolysis
- **Control Group**: Patients receiving ultrasound-guided induced abortion All subjects will be followed up for 2 years after the last case enrollment. Data including baseline demographics, follow-up imaging results and fertility outcomes during the follow-up period will be collected.

4. Inclusion and Exclusion Criteria

Inclusion Criteria

1. Early intrauterine pregnancy (normal or abnormal embryonic development, actual gestational age ＜14 weeks)
2. Ultrasonographic evidence of intrauterine adhesions or prior history of hysteroscopic adhesiolysis with clinical suspicion of active IUA
3. Planned hysteroscopic surgery or ultrasound-guided induced abortion

4. Postoperative pelvic ultrasound completed at our hospital with follow-up ultrasound data available for ≥3 months
5. Absence of severe systemic disorders

Exclusion Criteria

1. Ectopic pregnancy at atypical sites (cornual pregnancy, cesarean scar pregnancy, etc.)
2. Concurrent resection of other uterine lesions (endometrial polyps, adenomyosis, uterine septum, etc) during hysteroscopy (cervical canal procedures excluded)
3. Patients choosing medical abortion for pregnancy termination
4. Abnormal postoperative pathological findings (hydatidiform mole, gestational trophoblastic neoplasia, etc.)
5. No intrauterine adhesions identified intraoperatively during hysteroscopy

5. Sample Size Calculation

This study adopts a controlled design. The primary endpoint is the 30-month subsequent pregnancy rate. Based on previous retrospective controlled data from our research team, the subsequent pregnancy rate was 64.21% in the experimental group (p1) and 59.05% in the control group (p2). With a two-sided significance level $\alpha = 0.05$ and statistical power of 90%, PASS 2021 software was used for non-inferiority trial sample size calculation, yielding a required sample of 158 cases per group. Accounting for a 10% loss to follow-up and refusal to participate, at least 180 subjects are required for each group, with a total target sample size of 360 cases (180×2).

6. Research Procedures

1. All patients admitted to the Family Planning Ward with early pregnancy combined with IUA who intend to terminate pregnancy will be informed of study options and voluntarily select either hysteroscopic abortion with concurrent adhesiolysis or ultrasound-guided induced abortion. Eligible patients will be enrolled per inclusion and exclusion criteria.
2. Subjects receiving hysteroscopic combined surgery are assigned to the experimental group, while those receiving ultrasound-guided abortion form the control group; all enrolled patients will be followed up for 2 years.

3. Primary outcomes: subsequent pregnancy rate and fertility outcomes; Secondary outcomes: retained gestational tissue rate and IUA recurrence rate.
4. Data collection items: baseline demographics, age, obstetric history, fetal viability of current pregnancy, intraoperative blood loss, intrauterine anti-adhesion material placement, postoperative estrogen administration, tissue residual rate, IUA recurrence rate, postoperative fertility status, etc.
5. Moderate-volume decidual tissue will be collected postoperatively for immunohistochemical testing and cryopreservation for subsequent cytological research.

7. Statistical Considerations

Statistical descriptive indicators and analytical methods will be rationally selected according to research objectives, data types and distribution characteristics. All statistical tests are two-sided with $\alpha=0.05$; $P \leqslant 0.05$ is defined as statistically significant difference.

- Quantitative variables: described by mean, standard deviation, median, minimum and maximum values.
- Categorical and ordinal variables: described by constituent ratios, percentages or frequencies. Parameter estimation and hypothesis testing will be conducted for different analysis populations in accordance with the pre-specified statistical analysis plan.

8. Feasibility Analysis

1. The research team consists of cooperative and innovative investigators with rigorous scientific attitudes, multiple members have published SCI papers, providing solid human resources support for this project.
2. Extensive domestic and international literature review has been completed, laying sufficient theoretical foundation.
3. Ultrasonography achieves a diagnostic accuracy of over 90% for intrauterine adhesions, supporting reliable clinical diagnosis.
4. Clinicians at the study center are proficient in performing induced abortion and hysteroscopic surgery.
5. This is a prospective observational study without additional interventional measures imposed on subjects.
6. A retrospective preliminary study of this project has been completed, offering guidance and reference for the present research.

9. Ethical Considerations

This clinical trial will be conducted in compliance with the Declaration of Helsinki (2000), Good Clinical Practice (GCP) and relevant national regulatory requirements. Prior to study initiation, the full research protocol and supplementary documents shall be submitted to the Institutional Review Board (IRB) of the study hospital for ethical approval. Study implementation can only commence after formal IRB clearance. Any amendments to the research protocol must be re-approved by the IRB before implementation. All serious adverse events occurring during the trial shall be reported to the IRB in written form in a timely manner.