Official Title:
Retrospective Evaluation of the Effectiveness of Methotrexate Treatment in Cases with

Relative Contraindications in Ectopic Pregnancies

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Background and Justification of the Study

Ectopic pregnancy poses a significant risk in terms of maternal morbidity and mortality and accounts for approximately 1–2% of all pregnancies. With the advancement of early diagnostic methods, non-surgical treatment options have become more prominent; among these, systemic methotrexate therapy has emerged as a safe and effective alternative, particularly in selected patients. However, when selecting patients for methotrexate treatment, both absolute and relative contraindications that may affect treatment success must be carefully evaluated.

In the literature, data on the use of methotrexate in patients with relative contraindications are limited, and findings regarding treatment response, the rate of transition to surgery, and complications in this patient group remain unclear. This lack of clarity can lead to uncertainty in clinical decision-making.

In this study, the retrospective data of 238 patients diagnosed with ectopic pregnancy and treated with methotrexate at our institution, a training and research hospital, between 2019 and 2024 will be analyzed. The number of patients with relative contraindications and the criteria by which they were deemed eligible for methotrexate treatment will be determined during the analysis phase.

This retrospective observational study aims to identify the factors affecting treatment success, particularly in the group of patients with relative contraindications, thereby contributing to patient selection and management processes. By providing real-world data on current clinical practice, this research may also serve as a foundation for future prospective studies.

Purpose of the Study

The aim of this study is to retrospectively examine the clinical data of patients who were treated with methotrexate for ectopic pregnancy at a training and research hospital between 2019 and 2024, in order to evaluate treatment response rates and the factors affecting treatment success. In particular, by analyzing the effectiveness of methotrexate therapy in patients with relative contraindications, the rate of transition to surgical intervention, and complications arising during treatment, the study aims to more clearly determine the suitability of medical treatment for this patient group.

The hypothesis of the research is that methotrexate treatment may be effective and safe in ectopic pregnancy cases that meet appropriate criteria, even in the presence of relative contraindications. In addition, certain clinical and laboratory parameters—such as initial β-hCG levels, mass size, and the presence of fluid in the Douglas pouch—are anticipated to play a significant role in predicting treatment success.

Study Protocol Plan

Ethics approval for this study was obtained on May 15, 2025. This study is a retrospective, descriptive, and observational analysis conducted at a training and research hospital, evaluating the data of patients who received methotrexate treatment for ectopic pregnancy between 2019 and 2024. Clinical data of a total of 236 ectopic pregnancy cases treated with methotrexate will be assessed by reviewing the hospital information management system and patient records.

The study will include both patients who responded to methotrexate treatment and those who did not benefit from it and required surgical intervention. Detailed evaluations will be conducted on each patient's demographic characteristics, obstetric history, mode of delivery, history of previous ectopic pregnancy, methotrexate dosage and administration method, revision curettage procedures performed during treatment, laboratory findings such as hemogram and β-hCG, ultrasound findings including the identified ectopic focus and the presence of free fluid in the Douglas pouch, treatment duration, length of hospital stay, need for surgical intervention, time taken for β-hCG levels to become negative, and pre- and postoperative β-hCG levels in surgical cases.

Response to methotrexate treatment will be defined as observing the expected decline in β-hCG levels over time and the completion of the process without the need for surgical intervention. Characteristics of patients who did not respond to treatment and required surgery will be analyzed separately to identify potential predictors of treatment failure. Data will be analyzed using SPSS (or an appropriate statistical software), and in addition to descriptive statistics, significance tests will be applied to evaluate the relationship between various parameters and treatment success.

Statistical Analysis Plan

The analyses will be conducted using the GraphPad Prism 8 software. In cases where the dataset exhibits a normal distribution, parametric tests will be used. Parametric tests are more powerful than non-parametric tests. The normality of the distribution will be assessed using the Shapiro-Wilk test, the proximity of the mean and median values, and skewness and kurtosis criteria.

Since the groups exhibit normal distribution, **one-way analysis of variance (One-way ANOVA)** will be used for intergroup comparisons. For multiple comparisons, the **Dunnett test** will be used to compare each group to the control group, while the **Tukey's HSD test** will be used for comparisons among the other groups not including the control group.

A significance level of 0.05 will be adopted, and differences between means will be considered statistically significant with 95% confidence.