

Original Article:



Expectant Management Versus Drug Treatment with Oral Contraceptive Pills in the Elimination of Pregnancy Remnants Caused by Incomplete Spontaneous Abortion in the First Trimester of Pregnancy: A Randomized Clinical Trial

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Abstract

Introduction: Various medical, surgical, and recently expectant methods are being considered for the removal of the retained products of conception caused by incomplete abortion. We aimed to assess the effectiveness and safety of oral contraceptive pills (OCP) and expectant (waiting) methods in the successful removal of these remnants.

Materials and Methods: In this clinical trial, 58 patients were randomly treated with medication with OCPs, and the equivalent group of 58 patients were treated expectantly. The patients underwent treatment and intervention for three weeks, and then both groups underwent transvaginal ultrasound one week after the intervention to check whether they had successfully expelled the retained products of conception. The statistical software SPSS version 23.0 was used for the statistical analysis (IBM, Armonk, New York). P values of ≤ 0.05 were considered statistically significant.

Results: In terms of the success in removing the retained products from the abortion, this success in the two groups treated with OCP and expectant management were 84.5% and 86.2%, respectively, which did not show a difference between the two groups (p -value > 0.05). In terms of other outcomes after the intervention, including infection, bleeding, and abdominal pain, no significant difference was observed between the two groups (p -value > 0.05). There was no significant difference between the two groups in the duration of full recovery and return to daily activities (p -value > 0.05).

Conclusion: In the comparison of two medicinal methods regarding the complete disposal of abortion remnants, there is no difference in the success rate of the methods as well as the resulting complications including infection, pain, or bleeding. Also, the time to return to work and daily activities was similar in both groups.

Keywords: Abortion, oral contraceptive, expectant management, pregnancy.

1. Introduction

The overall estimate of abortion in Iran is 0.26 abortions per married woman, which means that every woman has less than one abortion on average during her reproductive life. The annual abortion rate is generally around 7.5 abortions per 1,000 married women aged 15 to 49 in Iran [1]. Early miscarriage is one of the common complications in pregnancy. Spontaneous abortion refers to the loss of an intrauterine pregnancy without external intervention before the 20th week of gestation, and accounts for about 20% of pregnancies [2]. Spontaneous abortion can be divided into subgroups of threatened abortion, unavoidable abortion, incomplete abortion, forgotten abortion, infectious abortion, complete abortion, and recurrent abortion [2]. Overall, about 25% of miscarriages are idiopathic. Chromosomal abnormalities – most commonly polyploidy and monosomy X – are the cause of nearly 50% of spontaneous abortions in the first trimester of pregnancy. Various other factors such as the underlying disease of the mother, disorders of the placenta and uterus, and glandular disorders are also considered as other causes of miscarriage [3]. Spotting or vaginal bleeding in the first trimester in a pregnant mother can be a sign of the beginning of the abortion process. Ultrasound plays a key role in diagnosis. In incomplete abortion, there is evidence of pregnancy remnants in transvaginal ultrasound despite the removal of pregnancy products. Women who experience complete spontaneous abortion rarely require medical treatment or surgical intervention [4]. However, for women with incomplete abortion, different treatment options are available. In patients with unstable vital signs, surgery is the treatment of choice, in which the patient undergoes evacuation of the remaining products of pregnancy or D&C (Dilation & curettage) [5]. In patients with stable vital signs, we are faced with more treatment options. New research has shown that expectant treatment, which means observing the patient until the complete removal of pregnancy remains for two weeks, has been associated with success without the patients suffering the complications of surgical interventions [6]. Among the treatment methods, many patients prefer antipyretic treatment, but it is necessary to mention that in the research conducted, the success rate of this treatment method in managing patients has been variable [7]. Another upcoming method in dealing with such patients is medical treatment using prostaglandin agonists. In this way, misoprostol alone or in combination with Mifepristone is used intravaginally, which has shown up to 80% success in research [6]. Considering the importance of pregnancy and its complications and its important effects on the

physical and mental health of people, care should be taken to adopt the appropriate treatment method in dealing with women who have experienced an unsuccessful pregnancy for any reason. Diagnosing abortion and its types, followed by choosing the correct treatment method, will not only guarantee the health of the mother, the society, maintain fertility and successful future pregnancies, but also reduce the dangerous complications that may endanger the lives of pregnant mothers [8]. Until now, there has been little research in this field that has compared different methods in the management of early miscarriage. In most of these studies, the success rate and side effects of each of the methods have been investigated alone, or two methods of expectant treatment and surgery have been compared. Also, among these, the number of clinical trials conducted has been very small [9, 10].

New research has proposed the use of Oral Contraceptive Pills (OCPs) as a potential aid in the removal of pregnancy remnants in incomplete abortion. However, only a limited number of studies have evaluated its effectiveness [10]. Surgical and medical methods are the available choices for the management of premature abortions (Premature abortion refers to the spontaneous or induced termination of pregnancy before the fetus reaches viability, typically before 20-24 weeks of gestation. It can result from genetic abnormalities, maternal health conditions, infections, or external factors), each of which has its advantages and disadvantages. In the last two decades, the efficacy and safety of expectant treatment have been proven. In this method, the patient is allowed to expel the remains of the failed pregnancy spontaneously [11, 12]. In this study, an attempt was made to investigate the two methods of expectant treatment and medical treatment using birth control pills in the elimination of pregnancy remnants in people who experienced a spontaneous but incomplete abortion in the first trimester of pregnancy. Also, the complications and success rate of each should be compared with each other.

2. Materials and Methods

Study population

The current study was a double-blinded randomized clinical trial, which started sampling after obtaining the approval of the ethics committee of the Iran University of Medical Sciences and receiving the code of ethics (ethical code: IRCT20220307054209N1) and was registered in the Iranian Registry for Clinical Trials (IRCT code: IRCT20220307054209N1, registration date: 01/08/2022). All experiments were performed in accordance with the Helsinki rules and guidelines. The statistical population in this study

included women referring to Shahid Akbarabadi Hospital in Tehran in 2022. Pregnant women whose intrauterine pregnancy was confirmed by abdominal or transvaginal ultrasound (early pregnancy) and who had a spontaneous abortion in the first trimester (with a gestational age of less than 12 weeks) were included in the study considering other inclusion criteria. In this regard, all women aged 15 to 45 years, who had a spontaneous abortion in the first trimester of pregnancy (under 12 weeks of pregnancy), had experienced an incomplete miscarriage, and in whom the presence of pregnancy remnants smaller than 4 cm was confirmed by transvaginal ultrasound, were eligible for the study. The remnants of pregnancy from their abortion were confirmed (less than 4 cm) and were the result of a failed intrauterine pregnancy; they had stable hemodynamics, and had no symptoms or mild vaginal spotting and bleeding. Those with unstable vital signs, suspected molar pregnancy, or contraindications to OCP were excluded from the study.

Study interventions

The intended intervention in this study was carried out in two groups in the first intervention group, expectant management along with oral contraceptive pills (OCPs) as a placebo for three weeks was considered, and in the second intervention group, medical treatment using contraceptive pills was considered for three weeks. Medical treatment was administered using an oral contraceptive pill containing 0.03 mg of ethinyl estradiol and 0.15 mg of levonorgestrel. The treatment commenced on the first day of residual tissue diagnosis and continued for 21 days. For randomization, after selecting qualified women and selecting samples, 116 people were selected. Then, 58 people were randomly placed in each group with a random selection of 1:1. An attempt was made to use block randomization as a random method. By using this method, we can be sure that confounding variables cannot affect the results. Blinding in this study was double-blind, so that the analyst and the person responsible for collecting the data were unaware of the intervention and the results in the two groups.

Study outcomes

The primary outcome of the study was the rate of success in removing pregnancy remnants in the two groups. One week after the end of the treatment period in both groups, both groups were again subjected to transvaginal ultrasound to check whether they succeeded in expelling the remnants of pregnancy or not. In this way, it was possible to compare the success rate of treatment methods between the two groups. It should be noted that the patients were examined regarding clinical symptoms such as the volume of bleeding (based on the number of pads used), the incidence of infection, the number of days required to return to daily activities, and the intensity of pain during follow-up.

Statistical analysis

For statistical analysis, results were presented as mean $\pm$ standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared using the t-test or Mann-Whitney test whenever the data did not appear to have a normal distribution or when the assumption of equal variances was violated across the study groups. The Chi-Square test or Fisher's exact test was used to compare the categorical variables. P-values of ≤ 0.05 were considered statistically significant. For the statistical analysis, the statistical software SPSS version 23.0 for Windows (IBM, Armonk, New York) was used.

3. Results

In the present study, initially, 60 patients were included who were randomly assigned to receive OCPs or a placebo. Of those, one patient in the first group and another patient in the placebo group discontinued the study protocol because of dissatisfaction with the study participation, and thus, 58 patients (29 patients in each group) were the final study participants [\[Figure 1\]](#).

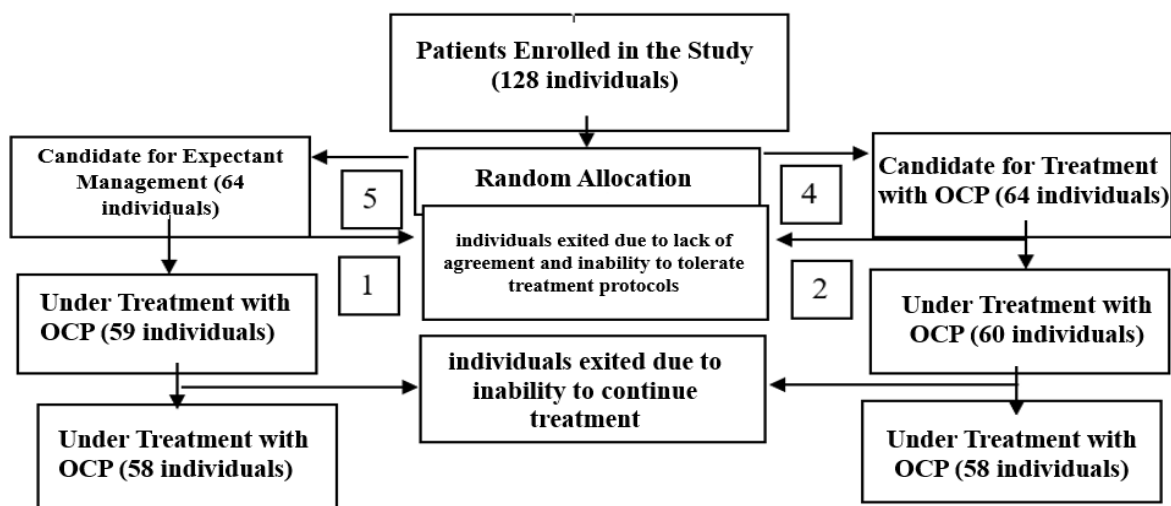


Figure 1. Flowchart depicting the study design and patient allocation.

Comparing baseline characteristics of the study population between the two groups [Table 1] showed no difference in mean age, gravida and parity, mean gestational age, mean body mass index, history of abortion, mean endometrial diameter, mean size of mass, and laboratory parameters including white blood cell count, serum hemoglobin level, and platelet count. Comparing the changes in laboratory parameters in each group showed no significant changes after the intervention. Also, no difference was revealed in each laboratory parameter after the intervention between the two interventional groups.

Regarding treatment outcomes in the two groups treated with OCP and expectant treatment with an

OCP placebo [Table 2], firstly, the rate of success in complete evacuation of abortion remnants was estimated to be 84.5% and 86.2%, respectively indicating no significant difference between the two groups ($P=0.793$). The number of days required to rest and start physical activity was also not different between the two groups. The frequency of abdominal pain after the intervention was 10.3% and 12.1%, which were similar between the two groups ($P=0.769$). The average pain score (based on the VAS system) was 2.16 ± 0.75 and 2.28 ± 0.76 , respectively, which did not differ between the two groups ($P=0.782$). Also, the frequency of bleeding cases after the intervention was 13.8% and 6.9%, respectively, which was similar between the two groups ($P=0.223$).

Table 1. Baseline characteristics in the study population

Characteristics	OCP group	Expectant group	P-value
Mean age, year	30.88±6.45	32.00±6.51	0.353
Mean body mass index	25.12±3.23	25.76±3.51	0.321
Mean gestational age, wk	10.50±1.63	10.31±1.71	0.543
Mean gravid	2.16±1.07	2.14±1.17	0.934
Parity			0.897
Nulipar	26 (44.8)	26 (44.8)	
Primipar	13 (22.4)	15 (25.9)	

Multipar	19 (32.8)	17 (29.3)	
History of abortion			0.743
One	48 (82.8)	49 (84.5)	
Two	9 (15.5)	7 (12.1)	
Three	1 (1.7)	2 (3.4)	
Mean endometrial thickness	14.33±4.78	13.75±4.71	0.507
The mean size of the mass	23.67±7.03	23.39±6.29	0.823
Mean WBC count	10193.10±6166.52	9160.34±2656.67	0.256
Mean hemoglobin level	12.63±1.29	12.30±1.19	0.153
Mean platelet count	242.83±64.16	227.03±52.32	0.149

Table 2. Studied outcome in the study population

Characteristics	OCP group	Expectant group	P-value
Success in complete evacuation of remnants	49 (84.5)	50 (86.2)	0.793
The number of days required to rest and start physical activity			0.304
One	41 (70.7)	48 (82.8)	
Two	15 (25.9)	9 (15.5)	
Three	2 (3.4)	1 (1.7)	
Infection	3 (5.2)	2 (3.4)	0.648
Abdominal pain	6 (10.3)	7 (12.1)	0.769
Mean pain score	2.16±0.75	2.28±0.76	0.782
Bleeding	8 (13.8)	4 (6.9)	0.223
Mean WBC count	9377.65±5673.65	8427.51±2444.13	0.256
Mean hemoglobin level	13.90±1.42	13.53±1.31	0.186
Mean platelet count	245.26±64.81	229.30±52.84	0.226

4. Discussion

The main effort of specialists is to completely remove the remnants caused by abortion to reduce its potential complications, especially the occurrence of infection, sepsis, and severe bleeding with excruciating abdominal pain. In this regard, various medical, surgical, and recent methods are being considered [3]. The latter method, i.e., waiting, has always been appreciated and welcomed due to the lack of direct interventions, its cost-effectiveness, the lack of patient anesthesia, or the absence of drug side effects, and it has been associated with mutual satisfaction of the patient and the doctor [1]. But whether this method can be a suitable alternative to surgical and medical methods is still a challenge. The present study aims to evaluate the effectiveness and safety of both OCP and expectant treatment in the successful removal of remnants from an incomplete abortion.

The study found that both OCP and expectant treatment were similarly successful in removing remnants from abortion, with success rates of 84.5% and 86.2% respectively. There was no significant difference in primary outcomes between the two groups. Additionally, there were no notable variations in secondary outcomes such as infection, bleeding, or abdominal pain, nor in the duration of recovery and return to daily activities. Both methods demonstrated comparable clinical outcomes and satisfactory levels of doctor and patient satisfaction. However, expectant treatment was preferred due to concerns about potential long-term side effects associated with OCP usage, making it less favorable despite similar efficacy. Therefore, the study suggests giving more attention to expectant treatment due to its similarity in clinical outcomes with fewer concerns about long-term side effects.

What has been discussed in the studies and has been discussed as findings regarding the consequences of various methods, the acceptability of the expectant method has been emphasized. In the study of Fernlund et al. [13], the aim was to compare the effectiveness of expectant treatment with vaginal misoprostol in patients with early incomplete abortion, in which the treatment rate in the two groups was 75% and 75%, respectively, which showed a significant difference between the two groups. In the study of Wada et al. [14], the success rate of expectant treatment was stated to be 77%. In the study of Mohammed K Ali et al. [15], cases of complete abortion were much higher in the misoprostol group than in expectant therapy (69% vs. 16.7%). Although the level of satisfaction in the

misoprostol group was higher than in the waiting group, the first group experienced more pain.

In Shelley et al.'s [16] study, cases of success in the complete disposal of abortion remains were equal to 80% in the drug method, 100% in the surgical method, and 78.6% in the expectant method. Cases of infection were reported in two patients in the drug group. There was no difference between the three groups in terms of pain, activity recovery, anxiety, or depression. In the study of Wijesinghe et al. [9], the success rate in the elimination of pregnancy remnants was 90.1% in the first week and 94.4% in the second week. In the study of Dangalla et al. [8], expectant treatment was successful in eliminating the remnants in the uterus in 69% of patients. In the study of Sajan et al. [7], the success rate in the surgical method was 97% compared to the expectant method of 71% and the patient satisfaction rate was 74% in the expectant treatment compared to 80% in the surgical method. Therefore, the range of success of the waiting method in the complete removal of abortion remnants is estimated between 65 and 94%, which suggests that our treatment group has faced high success. Also, due to the limited side effects after the treatment, this method can be an alternative option for medical or surgical intervention methods.

5. Conclusion

In conclusion, in the comparison of two medicinal methods (OCP) and expectant management regarding the complete disposal of abortion remains, no difference in the success rate of the methods, as well as the resulting complications, including infection, pain, or bleeding, was observed. Also, the time to return to work and daily activities was similar in both groups. Therefore, taking into account that in drug treatment, there will be an expectation of side effects in the long term, an alternative waiting method will be acceptable. This study contributes to the existing literature by directly comparing the effectiveness and safety of oral contraceptive pills (OCP) and expectant management in the removal of retained products of conception after incomplete abortion. Unlike previous studies, which primarily focused on surgical and medical (misoprostol) management, our research evaluates a less commonly studied approach—OCP—for this purpose. Additionally, our study provides a randomized comparison of OCP and expectant management, offering new insights into their success rates, complication profiles, and recovery times. The findings support that OCP is as effective as expectant management, with no significant difference in complications, thereby expanding the available non-surgical options for clinical practice.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of the Iran University of medical sciences (Code: IRCT20220307054209N1).

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Author's contributions

MR and MRS designed the protocol and supervised data collection, MK, FJ, and NJ collected the data, and ASH analyzed the data and drafted the manuscript.

Conflict of interest

The authors have no conflict of interest

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