Role of prophylactic antibiotics in preventing pelvic infection after surgical management of first-trimester miscarriage

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Abstract

Background: Prophylactic antibiotics have been traditionally used to prevent postoperative infection after surgical intervention for the first-trimester miscarriage. This work aims to study the role of prophylactic antibiotics in preventing pelvic infection after surgical management of first-trimester miscarriage.

Methods: This study was conducted on 138 women who underwent surgical management of first-trimester miscarriage. They were equally divided into two groups; the women in the study group were given a single dose of oral doxycycline (200 mg) and metronidazole (500 mg) 2 hours before the surgical procedure. The other group was given a placebo. Both groups were followed up for assessment of postoperative infection within two weeks.

Results: According to the original strict criteria, the prevalence of pelvic infection was found in 8.7% in the antibiotic group (6 out of 69) and 13% in the placebo group (9 out of 69), P=0.412. On follow-up, there was no significant difference between the studied groups concerning postoperative complications.

Conclusion: Prophylactic antibiotics before the surgical intervention of first-trimester miscarriage resulted in an insignificant decrease in postoperative pelvic infection.

Keywords: prophylactic antibiotics; pelvic infection; first-trimester miscarriage.

Introduction

Miscarriage is the termination of pregnancy before fetal viability (less than 20 weeks of pregnancy) or with a fetal weight of below 500 g, i.e., termination of pregnancy before the fetus is capable of extrauterine living (1). It is one of the commonest outcomes in pregnancy, accounting for about 25% of all pregnancies worldwide (2). If occurred within the first 13 weeks of gestation, it is called early or first-trimester miscarriage.

According to the American College of Obstetrics and Gynecology (ACOG), treatment options for miscarriage

include expectant, medical, or surgical management. Surgical options include aspiration and the traditional dilatation and curettage (D&C) (3). Currently, hysteroscopic management and ultrasound-guided surgical evacuation are superior to the blind evacuation technique (4).

The overall complication rate for surgical evacuation of the uterus is approximately 6%. Complications include bleeding, infection, retained placental or fetal tissue, intrauterine adhesions, perforation, and cervical trauma. Up to 30% of women in low-income countries get a pelvic infection after miscarriage surgery, which can have substantial consequences for morbidity and death. National and international guidelines on the surgical management of miscarriage advocate using prophylactic antibiotics to reduce the risk of infection (5).

The localized pelvic infection has been reported in up to 40 in 1000 women after surgical evacuation. According to the Royal College of Obstetrics and Gynecology (RCOG), routine use of prophylactic antibiotics at the time of surgical management of miscarriage is the best practice as it reduces the risk of infection after the procedure (6).

However, current recommendations do not suggest the use of antibiotics prior to miscarriage surgery unless there is evidence of infection since there is insufficient data to support the regular use of antibiotic prophylaxis in the surgical management of miscarriage (5). There are conflicting international recommendations for antibiotic prophylaxis before surgery for incomplete spontaneous abortion. Due to a lack of proof of their effectiveness, some people do not advise using antibiotics (5). So, we aimed to determine the role of prophylactic antibiotics in preventing pelvic infection after the surgical management of miscarriage.

Methods

This clinical trial was conducted at Kasr El-Ainy university hospital and Bolak hospital from January 2021 to May 2022, during which about 138 women were included for management of early miscarriage. The study was approved by the ethical committee of the Gynecology and Obstetrics and was registered at the Clinical trial.gov (registration no. NCT05167838).

The included women had signed written informed consent before participating in this study after being informed of the purpose, interventions, outcome, and possible complications.

Inclusion criteria were female patients between 18 and 35 years old with singleton miscarriage (incomplete or missed), gestational age less than 13 weeks (confirmed by a reliable date for the last menstrual period or/and first-trimester ultrasound scan), and being subjected to the surgical management within two weeks of diagnosis of miscarriage. Women were excluded if they had induced or septic miscarriage, any evidence of infection, morbid obesity (BMI $\geq$40 kg/m^2), or allergy to prophylactic antibiotics (i.e., doxycycline or metronidazole). Women were also excluded if antibiotics were given within 7 days before randomization.

Women were randomly distributed into two equal groups; the study group (Group A), in which women received prophylactic antibiotics (single dose of oral doxycycline 200 mg and metronidazole 500 mg) 2 hours before the surgical management, and the control group (Group B), in which women received placebo 2 hours before the surgical management. Randomization was done via random numbers generated using Microsoft Excel software, while masking was done using 138 identical envelopes, half of them filled with the label "Group A", while the other half filled with the label "Group B". All envelopes were prepared by the investigator and sealed before starting enrollment. After enrollment, each participant was allowed to choose one envelope to determine which group was assigned.

All women in both groups were subjected to detailed history and clinical examination to ensure adherence to inclusion criteria. Vaginal ultrasound was done to confirm the diagnosis of miscarriage and its type. Routine laboratory tests were done, including complete blood count (CBC), coagulation profile (PT, PC, INR), c-reactive protein (CRP), liver functions (ALT, AST), and kidney functions (Creatinine). All patients underwent surgical management in the form of surgical evacuation or dilatation and curettage (D&C). Patients were followed at regular visits on the 5th, 10th, and 15th day of the postoperative period regarding the change in the vital signs and the laboratory tests.

Pelvic infection was diagnosed upon the presence of two of the following clinical parameters: purulent vaginal discharge, pyrexia (>38°C), uterine tenderness, white cell count > 12000 cells /mL^3, and the need for administration of antibiotics for the management of presumed pelvic infection.

Sample size calculation: Sample size was calculated by comparing the incidence of post-abortive pelvic infection between women undergoing surgical evacuation and given prophylactic antibiotics and those not given antibiotic prophylaxis. The calculation was based on comparing two proportions

from independent samples using the Chi-square test, the α-error was set at 0.05, and the study power was set at 80%. According to Goranitis et al. (2019), the incidence of pelvic infection after surgical evacuation in the non-treated high-risk group was approximately 43% (5), and we assumed that using prophylactic antibodies is expected to achieve a 50% reduction in this incidence, the optimum sample size should be 69 participants in each group.

Statistical methods: Statistical analysis was done using the statistical package for the Social Sciences (SPSS) version 25 (IBM Corp., Armonk, NY, USA). Data were summarized using mean ±standard deviation or number of cases with percentages. The independent samples t-test was used to compare groups regarding the quantitative variables, while the Chi-square test was for to compare the categorical variables. P-values < 0.05 were considered statistically significant.

Results

Patients were distributed into two groups; the study group (n=69), in which women received prophylactic antibiotics (single dose of oral doxycycline 200 mg and metronidazole 500 mg) 2 hours before the surgical management, and the control group (n=69), in which women received placebo 2 hours before the surgical management. There was no statistically significant difference between the two groups regarding the demographic and clinical characteristics, as shown in Table 1.

Table 1: Demographic and clinical characteristics of all patients

	Antibiotics group (n=69)	Placebo group (n=69)	p-value
Age	28.32 ± 5.24	28.75 ± 5.42	0.633
BMI	29.13 ± 4.32	28.13 ± 3.69	0.146
Parity	1.90 ± 1.15	1.88 ± 1.26	0.944
Previous mode of delivery - Nullipara - Previous NVD - Previous CS	 11 (15.9 %) 20 (29 %) 38 (55.1 %)	 10 (14.5 %) 31 (44.9 %) 28 (40.6 %)	0.140
Previous abortions	0.68 ± 0.89	0.71 ± 0.94	0.854

Medical History - Free - Hypertension - DM - Hyperthyroidism - Hypothyroidism - Antiphospholipid	 55 (79.7 %) 9 (13 %) 3 (4.3 %) 1 (1.4 %) 1 (1.4 %) 0	 55 (79.7 %) 7 (10.1 %) 3 (4.3 %) 0 3 (4.3 %) 1 (1.4 %)	0.662
Current G.A.	8.99 ± 1.68	8.94 ± 1.58	0.876
Type of abortion - Missed - Incomplete	 42 (60.9 %) 27 (39.1 %)	 37 (53.6 %) 32 (46.4 %)	0.390

Table 2 compares the antibiotics and placebo groups regarding the management procedure, the occurrence of postoperative bleeding, and the prevalence of pelvic infection. The surgical management was in the form of either surgical evacuation or dilatation and curettage (D&C) and showed no significant difference between the two groups (P=0.306). There was no significant difference between both groups regarding the bleeding that occurred postoperatively on days 0, 5, 10, and 15 (P=0.430, 0.196, 0.079, 0.116, respectively). According to the original strict criteria, pelvic infection was diagnosed in 8.7% in the antibiotic group (6 out of 69) and 13% in the placebo group (9 out of 69); P= 0.412. There is no privilege to use prophylactic antibiotics before the surgical intervention.

Table 2: Management of both groups and postoperative sequelae

	Antibiotics group (n=69)	**Placebo group (n=69)**	**p-value**
Procedure of management - D&C - Surgical evacuation	 40 (58 %) 29 (42 %)	 34 (49.3 %) 35 (50.7 %)	0.306
Bleeding on procedure day - No bleeding - Mild bleeding - Moderate bleeding - Severe bleeding	 8 (11.6 %) 34 (49.3 %) 16 (23.2 %) 11 (15.9 %)	 11 (15.9 %) 31 (44.9 %) 21 (30.5 %) 6 (8.7 %)	0.430
Bleeding on after 5 days - No bleeding - Mild bleeding - Moderate bleeding - Severe bleeding	 13 (18.8 %) 42 (60.9 %) 14 (20.3 %) 0	 16 (23.2 %) 46 (66.7 %) 6 (8.7 %) 1 (1.4 %)	0.196
Bleeding on after 10 days - No bleeding - Mild bleeding - Moderate bleeding	 39 (56.5 %) 28 (40.6 %) 2 (2.9 %)	 50 (72.5 %) 19 (27.5 %) 0	0.079
Bleeding on after 15 days - No bleeding - Mild bleeding	 61 (88.4 %) 8 (11.6 %)	 66 (95.7 %) 3 (4.3 %)	0.116
Pelvic infection (Two signs) - Pelvic infection - No pelvic infection	 6 (8.7 %) 63 (91.3 %)	 9 (13 %) 60 (87 %)	0.412

The vital signs and laboratory results in both groups were recorded on the day of surgical management and on the 5th, 10th, and 15th days postoperative. Table 3 demonstrates these changes that occurred in each group. Overall, there is no significant difference between both groups regarding the change in blood pressure, pulse, temperature, Hb level, total leukocytic count, platelets count, coagulation profile (PT, PC, INR), c-reactive protein (CRP), liver functions (ALT, AST), and kidney functions (Creatinine).

Table 3: Changes in the vital signs and laboratory findings

	Antibiotics group (n=69)	Placebo group (n=69)	p-value
Change in Blood pressure			0.513
- Decreased	22 (31.88 %)	16 (23.19 %)	
- No Change	14 (20.29 %)	15 (21.74 %)	
- Increased	33 (47.83 %)	38 (55.07 %)	
Change in pulse			0.314
- Decreased	45 (65.22 %)	53 (76.81 %)	
- No Change	10 (14.49 %)	6 (8.70 %)	
- Increased	14 (20.29 %)	10 (14.49 %)	
Change in temperature			0.119
- Decreased	32 (46.38 %)	23 (33.33 %)	
- No Change	24 (34.78 %)	36 (52.17 %)	
- Increased	13 (18.84 %)	10 (14.49 %)	
Change in Hb			0.871
- Decreased	55 (79.71 %)	53 (76.81 %)	
- No Change	2 (2.90 %)	3 (4.35 %)	
- Increased	12 (17.39 %)	13 (18.84 %)	
Change in WBCs			0.729
- Decreased	60 (86.96 %)	57 (82.61 %)	
- No Change	1 (1.45 %)	2 (2.90 %)	
- Increased	8 (11.59 %)	10 (14.49 %)	
Change in platelets			0.086
- Decreased	40 (57.97 %)	27 (39.13 %)	
- No Change	2 (2.9 %)	3 (4.35 %)	
- Increased	27 (39.13 %)	39 (56.52 %)	
Change in CRP			0.930
- Decreased	50 (72.46 %)	50 (72.46 %)	
- No Change	15 (21.74 %)	14 (20.29 %)	
- Increased	4 (5.80 %)	5 (7.25 %)	
Change in PT			0.950
- Decreased	49 (71.01 %)	49 (71.01 %)	
- No Change	9 (13.04 %)	8 (11.59 %)	
- Increased	11 (15.94 %)	12 (17.39 %)	
Change in PC			0.782
- Decreased	38 (55.07 %)	34 (49.28 %)	
- No Change	4 (5.80 %)	5 (7.25 %)	
- Increased	27 (39.13 %)	30 (43.48 %)	

Change in INR - Decreased - No Change - Increased	 45 (65.22 %) 18 (26.09 %) 6 (8.70 %)	 44 (63.77 %) 21 (30.43 %) 4 (5.80 %)	0.725
Change in ALT - Decreased - No Change - Increased	 33 (47.83 %) 2 (2.90 %) 34 (49.28 %)	 40 (57.97 %) 4 (5.80 %) 25 (36.23 %)	0.258
Change in AST - Decreased - No Change - Increased	 29 (42.03 %) 11 (15.94 %) 29 (42.03 %)	 40 (57.97 %) 5 (7.25 %) 24 (34.78 %)	0.107
Change in creatinine - Decreased - No Change - Increased	 34 (49.28 %) 16 (23.19 %) 19 (27.54 %)	 38 (55.07 %) 8 (11.59 %) 23 (33.33 %)	0.195

Discussion

Globally, an estimated 23 million miscarriages occur every year (7). Moradinazar et al. estimated the lifetime prevalence of abortion in 4831 women aged 35 to 65 years who participated in Ravansar Non- Communicable Disease (RaNCD) cohort study and gave birth. They found that 25.7% of patients experienced spontaneous abortion

(8). Unfortunately, many of these abortions become incomplete and require surgical intervention to complete the evacuation of the uterine components (9). This type of surgery is considered one of the most common operations in the field of obstetrics and gynecology.

Infection is one of the most common complications that occur postoperatively in cases with surgical miscarriage. It may lead to increased morbidities and mortalities; that may even end with death (10). That is why there was a debate concerning the use of preoperative antibiotic prophylaxis to decrease the incidence of postoperative infection. Some authors were with, and others were against and preferred not to use antibiotics preoperatively due to lack of evidence (3).

So, we tried to investigate the role of preoperative antibiotic prophylaxis in the prevention of postoperative complications of abortion. One hundred thirty-eight patients were included in the study. They were randomized into two groups, group A, including 69 participants who were given a single dose of oral doxycycline 200 mg and metronidazole 500 mg 2 hours before the surgical management, and group B, including 69 participants who were given placebo tablets before their operation.

We found that pelvic infection occurred in 10.9% of all patients. Although its prevalence was 6 out of 69 patients in the antibiotic group (8.7%) versus 9 out of 69 patients in the placebo group (13%), this ratio was statistically insignificant. This nearly matches what was found by Lissauer et al., who conducted a double-blinded placebo-controlled trial including 3412 patients who were admitted for first-trimester abortion. They were given a combination of oral metronidazole and oral doxycycline and followed up for 14 days to develop postoperative signs of infection. They found that 4.1% of patients in the antibiotic group compared to 5.3% of the other group developed infection postoperatively with no significant difference between both groups at the end of follow-up (11).

Titapant did another trial in 2012; they included 84 patients who were randomly assigned into one of two groups; the intervention one was given 1 g of cefoxitin as the source of preoperative antibiotic. They were followed up for one week postoperatively. They found that postoperative infection accounted for only 2 cases in the control group compared to no cases in the antibiotic group. However, this was also statistically insignificant (12).

On the other hand, Islam et al. performed a systematic review on 16178 participants from 24 RCTs. They found that antibiotic prophylaxis was effective in reducing the rate of postoperative genital tract infections (RR 0.72, CI 0.58: 0.90). However, these results were only marked in high-income countries but not significant in low and middle-income countries due to lack of evidence in these countries (13).

It is known that bleeding is one of the most common postoperative complications, whether primary or secondary. Our study found that postoperative bleeding was not significantly obvious among patients in both groups. This may be explained by the fact that the surgical induction of abortion results in minimal blood loss. On the other hand, medical induction of abortion was associated with heavier and prolonged bleeding, which significantly decreased the hemoglobin level (14).

Concerning obesity, we found in our study that the mean BMI for all patients was

28.63 ± 4.04 kg/m^2 lying in the category of overweight and obesity. This matches what we found in the literature. Benson et al. studied 4968 women undergoing surgical induction of abortion between September 2012 to July 2014 and found that 25% of patients were obese, in addition to 4% who suffered from morbid obesity. However, they could not establish a causality relationship between obesity and abortion due to the insufficiency of presented data (15).

No doubt that maternal age affects the outcome of pregnancy. Many researchers stated that increasing maternal age could lead to many adverse effects, e.g., gestational diabetes, congenital abnormalities, stillbirth, and even miscarriage (16). Khalil et al. reviewed 76158 cases presented for routine antenatal care to 3 UK hospitals and found that the risk of abortion increased with increasing maternal age at pregnancy, with the highest percentage occurring in more than 35 years old pregnant females (17).

In our study, we found that the mean age of patients who underwent surgical abortion was

28.54 ± 5.32 years old, with no significant difference between both studied groups. This was similar to what was found by Meaidi et al., who followed up patients who underwent surgical induced abortion between 2005 and 2015 and found that gestational age between

25 and 29 years old was significantly associated with a higher incidence of early abortions (18).

Conclusion

Prophylactic antibiotics before surgical management of first-trimester miscarriage resulted in an insignificant decrease in postoperative pelvic infection after 15 days of follow-up. We recommend performing this study on a larger number of patients for longer follow-up periods.

Declarations

Competing interests: The author has no financial or other conflicts of interest.

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Informed consent: All participants gave their consent after being informed of the study's objective and design, and they were given the option to leave the study at any time.

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