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Original research article

What happens when we routinely give doxycycline to medical abortion patients?☆,☆☆

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Abstract

Objectives: Routine provision of antibiotics following medical abortion is common yet practitioners and professional societies differ on its utility. Our study compares the side effects experienced by women who were prescribed doxycycline following medical abortion to those who were not and assesses the adherence to one prescribed regimen.

Study design: This was a prospective, observational, open-label study from a convenience sample. Women seeking medical abortion were enrolled in nine study sites, including four clinics that routinely prescribe a seven-day course of doxycycline (Doxycycline arm) and five clinics that do not routinely prescribe any antibiotics (No Doxycycline arm). Seven to fourteen days following the administration of mifepristone, women were asked to self-administer a computer-based survey. The survey asked about side effects experienced (both arms) and adherence to the regimen (Doxycycline arm only).

Results: Five hundred eighty-one women were enrolled (278 in the Doxycycline arm and 303 in the No Doxycycline arm). There was a trend toward increased nausea in the Doxycycline arm (47.8% vs. 40.9%; p=.056) and a statistically significant difference in vomiting (25.2% vs. 18.5%; p=.032). Almost all women in the Doxycycline arm reported taking at least one pill, however only 28.3% reported "perfect adherence." The most common reasons reported for taking fewer pills than instructed were that participants were still taking them (beyond 7 days) or that they forgot to take them.

Conclusion: Women who were prescribed doxycycline following medical abortion reported moderate adherence and experienced significantly more vomiting than their counterparts.

Implications: In the absence of robust evidence that prescribing 7 days of doxycycline following medical abortion is effective at reducing serious infections, these data can assist the public health community with deciding whether routine provision is the most appropriate strategy.

Keywords: Antibiotics; Doxycycline; Mifepristone; Misoprostol; Infection; Compliance

1. Introduction

Early first trimester medical abortion is effective [1,2], highly acceptable to women [3–7], and safe [2,8,9]. The risk of infection following medical abortion is small, at less than 1% [10], with the rate of serious infection even lower, at .06/1000 [11].

Between 2001 and 2005, five women who had medical abortions in North America were infected with *Clostridium sordellii* bacteria which caused toxic shock-like illness and death [12–14]. Although these fatal infections were extremely rare and no link was established between medical abortion and clostridia infection, Planned Parenthood Federation of America (PPFA) was prompted by these deaths to change its medical abortion protocols in 2006 to replace vaginal with buccal administration and to require routine antibiotic coverage [15]. These changes were widely adopted across the United States even among many independent providers.

A retrospective review of data from PPFA showed a decrease over time in the serious infection rate after medical abortion following these protocol changes [11]. However, a subsequent report suggests that finding may have been a period effect [16,17]. Clifford and Daley estimated from the earlier PPFA data that 2500 women would need to be treated

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with antibiotics for a week to prevent one serious infection, and concluded that antibiotic prophylaxis for medical abortion is not warranted [18]. Indeed, recommendations from the World Health Organization, the Society of Family Planning, the American College of Obstetricians and Gynecologists, the National Abortion Federation, and the United States Food and Drug Administration all do not support routine use of preventive antibiotics for medical abortion [19–23]. To be clear, there is robust evidence of the efficacy of routine antibiotic prophylaxis following surgical abortion; however no clinical trials provide the same evidence base for medical abortion.

Despite the lack of conclusive evidence on the efficacy of routine antibiotic treatment following medical abortion, this practice is common [24]. Considering that over 85,000 medical abortions are performed in the US each year, the advantages and disadvantages of any associated routine practice are amplified. At the time the study was conducted, doxycycline was the most widely used antibiotic following medical abortion and was typically given in a seven-day treatment dose of 100 mg twice daily. This treatment does not come without costs financially, logistically, and in terms of side effects. Doxycycline is associated with gastrointestinal, skin, and urogenital side effects [25] and while allergy is rare, it can include hypersensitivity syndrome reaction and serum sickness-like reaction [26].

Difficulty adhering to any antibiotic regimen would have implications for the benefits of routine prescription. Extensive evidence suggests that patient compliance with antibiotics is low [27,28]. A study of patients treated with doxycycline for *Chlamydia* found that 16% of patients fully adhered (as measured by electronic pill bottle cap) and 67% of patients had at least one instance of 24 h between doses [29]. While beyond the scope of this paper, public health concerns around the overuse of antibiotics and the development of antimicrobial resistance are important when examining the pros and cons of routine provision [30].

In summary, robust evidence is lacking on the effectiveness of doxycycline treatment following medical abortion but most women in the US receive it. This study seeks to add to the literature evidence of the side effects women experience with post-abortion doxycycline treatment and their adherence to the regimen.

2. Materials and methods

This was a non-randomized, observational study conducted from October 2012 to December 2013. Participants were recruited from 9 clinics in the United States. Four clinics routinely prescribed doxycycline following medical abortion and five did not. All sites scheduled follow up visits at seven days following administration of mifepristone and, in the doxycycline arm, all sites dispensed the doxycycline directly to participants who were counseled to start the doxycycline the day they took mifepristone. Sites prescribed ancillary medicines (analgesics, antiemetics, etc.) according to their regular protocols or patient needs.

Women presenting for a medical abortion in the study clinics who could read English or Spanish were eligible for the study. Any woman who was currently taking antibiotics for reasons unrelated to her medical abortion was excluded as was any woman who had previously participated in this study.

On the day they took their mifepristone in the clinic, eligible women were provided with a study information card which listed a unique Study ID number and a website where they could access a computer-based questionnaire 7–14 days later. Women could take the questionnaire either at the clinic during their follow-up visits, or off-site wherever they had an internet connection. If participants chose to take the questionnaire at the follow-up visit, they were given a laptop to self-administer it in a private location. Women who did not return for follow-up were called and reminded of the possibility of participating in the study using the website and Study ID provided to them.

A woman was considered to be enrolled in the study once she accessed the website and gave her informed consent. The questionnaire used DatStat Illume v. 4.11 software and took 5–10 minutes to complete.

The survey contained questions on demographics, medications dispensed or prescribed, side effects experienced and adherence to the doxycycline regimen (Doxycycline arm only). All questions related to the time period between taking the mifepristone in the clinic and the date of survey administration (7–14 days later).

Women were provided with a list of side effects including: nausea, headache, vomiting, diarrhea, fever/chills, allergic reaction (rash, itching, wheezing) and yeast infection. They were asked to check each side effect experienced and had the option of writing in any others. We did not consider pain or bleeding to be side effects as they are the main effects of treatment. For each side effect women reported they were asked the severity, duration, and whether they took medications to treat it.

In the Doxycycline arm, adherence was measured by asking the dates when women started and stopped taking doxycycline, if any doses were missed, if two consecutive doses were missed, and the number of pills remaining at the time of survey completion. All women who took fewer pills than prescribed were asked to provide a reason. “Perfect adherence” was defined as not missing any doses, having 0 or 1 pill remaining at the follow-up visit, and taking the medicine for 7 or 8 days. Women were also asked about elements of antibiotic counseling they received. No information on infection rates was obtained as the goals of the study were to focus on adherence and side effects of a commonly used antibiotic regimen.

A sample size of 610 women (305 in each group) would be sufficient for a one-sided test to detect with 80% power a 10% lower nausea rate in the No Doxycycline arm (assuming a 50% nausea rate in the Doxycycline arm) [31]. A sample size of 305 in the Doxycycline arm would also allow an estimation of