ELSEVIER

Contraception 89 (2014) 193 – 196

Contraception

Original research article

Reduction in infection-related mortality since modifications in the regimen of medical abortion☆,☆☆,★

James Trussell[a,b,*], Deborah Nucatola[c], Mary Fjerstad[d], E. Steve Lichtenberg[e]

[a]Office of Population Research, Princeton University, Princeton, NJ 08544, USA
[b]The Hull York Medical School, University of Hull, Hull HU6 1RX, England
[c]Planned Parenthood Federation of America, New York, NY 10001, USA
[d]WomanCare Global, San Diego, CA 92122, USA
[e]Northwestern University Feinberg School of Medicine, Chicago, IL 60611, USA

Received 25 September 2013; revised 19 November 2013; accepted 24 November 2013

Abstract

Background: From 2001 to March 2006 Planned Parenthood health centers throughout the United States provided medical abortion by a regimen of oral mifepristone followed 24–48 h later by vaginal misoprostol. In response to concerns about serious infections, in early 2006 Planned Parenthood changed the route of misoprostol administration to buccal and required either routine antibiotic coverage or universal screening and treatment for chlamydia; in July 2007, Planned Parenthood began requiring routine antibiotic coverage for all medical abortions.
Methods: We performed a retrospective analysis of Planned Parenthood cases assessing the rates of mortality caused by infection following medical abortion during a time period when misoprostol was administered vaginally (2001 through March 2006), as compared with the rate from April 2006 to the end of 2012 after a change to buccal administration of misoprostol and after initiation of new infection-reduction strategies.
Results: The mortality rate dropped significantly in the 81-month period after the joint change to (1) buccal misoprostol replacing vaginal misoprostol and (2) either sexually transmitted infection (STI) screening or routine preventative antibiotic coverage (15 month period) or universal routine preventative antibiotic coverage as part of the medical abortion (66-month period), from 1.37/100,000 to 0.00/100,000, P=.013 (difference=1.37/100,000, 95% CI 0.47–4.03 per 100,000).
Conclusion: The infection-caused mortality rate following medical abortion declined by 100% following a change from vaginal to buccal administration of misoprostol combined with screen-and-treat or, far more commonly, routine antibiotic coverage.
Significance: Deaths from infection following medical abortion declined to zero after a change in the regimen.

Keywords: Medical abortion; Mortality; Doxycycline; Buccal misopristol; Clostridia

1. Introduction

Planned Parenthood Federation of America is a federation of 71 independent local affiliates operating 738 health centers throughout the United States; 332 now provide medical abortion. In 2012, 132,653 women received medical abortions, representing ~40% of first-trimester abortions in Planned Parenthood health centers.

Antibiotics have been routinely administered at the time of surgical abortions since the publication of a meta-analysis demonstrating that their use resulted in a 42% reduction in post-abortion infection rates (RR=0.58, 95% CI 0.47–0.71) [1]. When medical abortion was first introduced, infection risk was believed to be low and lower than for surgical abortion because the method was not invasive of the uterus (unless the procedure fails, when follow-up uterine evacuation is required). However, it is clear that serious infections do occur, albeit infrequently [2–5].

☆ Funding: This work was supported in part by the Eunice Kennedy Shriver National Institute of Child Health and Human Development grant for Infrastructure for Population Research at Princeton University, Grant R24HD047879 (JT).
☆☆ Disclaimer: The findings and conclusions in this presentation are those of the authors and do not necessarily represent the views of Planned Parenthood Federation of America.
★ Disclosures: The authors report no financial conflicts of interest.
* Corresponding author.
E-mail address: trussell@princeton.edu (J. Trussell).

0010-7824/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.contraception.2013.11.020

Between 2001 and late 2005, four women in the United States and one in Canada had died from a rare bacterial infection, *Clostridium sordellii,* following medical abortion with mifepristone and misoprostol; [6] an additional death occurred in the United States in early 2006 from *Clostridium perfringens*. In contrast, no such deaths had been reported in Europe, where medical abortion had been available longer and far more women had used it. One hypothesis for the difference was that vaginal administration of misoprostol was very common in the United States but not as common in Europe [7]. Another hypothesis was that peri-procedural antibiotics were very commonly provided in the United Kingdom but not in the United States. A final hypothesis is that deaths did occur but were not reported. These infections are rare; little is known about the epidemiology except that women are at highest risk of *C. sordellii* following the end of pregnancy (live birth, medical or surgical abortion, or spontaneous abortion [8].

Prompted by the deaths following medical abortion and internal data showing a higher than expected serious infection rate (4.5 times the previously published serious infection rate from Planned Parenthood data of 2 per 10,000 [5]), Planned Parenthood changed its medical abortion protocol at the end of March 2006. Vaginal administration of misoprostol was discontinued and replaced by buccal administration, and all health centers were required to use one of two strategies intended to reduce the risk of infection: either routine antibiotic coverage or universal screening for chlamydia (and for gonorrhea when considered appropriate), with treatment dependent on test results. After reviewing serious infection rates among health centers using these two different infection-reduction strategies, Planned Parenthood in July 2007 required all health centers to provide routine antibiotic coverage. This report compares rates of mortality before and after these changes.

2. Materials and methods

We studied patients having medical abortion at all Planned Parenthood affiliates providing this service at any time during the entire study period 2001–2012. Since 2001, affiliates have reported quarterly the number of patients receiving a medical abortion to the Coalition of Abortion Providers (CAPS) of Planned Parenthood affiliates.

The provisions of Food and Drug Administration (FDA) approval required any physician who orders, provides, or supervises the provision of mifepristone to sign an agreement with the sole US distributor of mifepristone (Danco Laboratories) to report all serious adverse events associated with its use [9]. Serious adverse events include hemorrhage requiring emergency treatment, serious infections, hospitalizations, potentially life-threatening events, and deaths. Danco submits all such reports to the FDA. Planned Parenthood staff was trained in accurate and complete reporting of serious adverse events. Adverse event reports are centrally tracked and monitored by the Coalition of Abortion Providers (CAPS) of Planned Parenthood affiliates.

After March 2006, Planned Parenthood changed the route of administration of misoprostol to buccal (200 mg of mifepristone followed 24–48 hours later by 800 μg of buccal misoprostol). In addition, Planned Parenthood health centers providing medical abortion were required either to (1) screen all patients for chlamydia (and gonorrhea if endemic rates or patient history or symptoms indicated need) or (2) provide routine antibiotic coverage with doxycycline orally 100 mg BID for 7 days, starting the same day as mifepristone administration. Doxycycline was chosen because it treats chlamydia, the most commonly reported sexually transmitted infection in the United States, and most gonorrhea strains [10], and provides protection against other organisms that cannot reasonably be tested for. The regimen is not prophylaxis; it was deliberately chosen as a treatment regimen; an antibiotic that specifically targeted *Clostridium* was not chosen. Patients who had a positive test for a sexually transmitted infection were treated with the standard US Centers for Disease Control and Prevention (CDC) treatment recommendations at that time, consisting of doxycycline orally 100 mg b.i.d. for 7 days for chlamydia, and ceftriaxone 125 mg intramuscularly in a single dose for gonorrhea.

We analyzed deaths due to infection for the years 2001 to 2012 over two time periods. Period 1 (January 1, 2001–March 31, 2006) was the baseline 63-month period during which vaginal misoprostol and standard antiseptic measures (hand washing before inserting vaginal misoprostol) were used for medical abortion through 49 (2001-mid 2002) or 63 (mid 2002-March 31, 2006) days of gestation. During this period a few affiliates decided to screen and treat for STIs based on CDC guidelines. Period 2 (April 1, 2006–December 31, 2012) was the 81-month period during which buccal misoprostol was used through 56 (April 1, 2006–December 31, 2007) or 63 (2008–2012) days of gestation [11]. From April 1, 2006 to June 30, 2007, a period of 15 months, some Planned Parenthood clinics used the infection-reduction strategy of universal STI screening and treatment when screening was positive, while others provided routine antibiotic coverage consisting of oral doxycycline 100 mg BID for 7 days. Rates of serious infection declined significantly in both groups, but the decline was significantly greater in the routine antibiotics group [12]. Consequently, from July 1, 2007, to the end of 2012, a period of 66 months, routine antibiotic coverage was universally provided (in the group that initially adopted screen-and-treat, there was a further significant drop in the serious infection rate in the second half of 2007 to the same level observed in the group that initially adopted routine antibiotic coverage [12]). Rates of mortality due to infection were compared in the two periods.

Fisher's exact test was used to assess the significance of differences in proportions. Calculations were performed in StatXact (Cytel Inc, Boston Massachusetts).The Princeton Institutional Review Board approved the study protocol and design as a retrospective analysis of data routinely collected for quality control.