Intravaginal metronidazole prior to cesarean section reduced the risk of postpartum endometritis


OBJECTIVE

To determine if intravaginal metronidazole, administered prior to cesarean section, reduces the risk of postpartum endometritis.

DESIGN

Randomized, double-blind, placebo-controlled trial. Allocation was computer-generated and carried out using coded medications prepared by the pharmacy.

SETTING

Tertiary care hospital in the USA.

SUBJECTS

224 women, mean age 26 years, who were about to undergo cesarean delivery at ≥24 (mean 38) weeks gestation. Women with chorioamnionitis were excluded. Eighty-eight per cent of women had intact membranes at admission and 58% experienced labour prior to
delivery. The main indications for cesarean delivery were elective repeat (34%), malpresentation (20%), arrest of dilation (15%), and fetal distress (13%). An additional 37 randomized women (14%) were excluded from the analysis because of protocol violations.

INTERVENTION

112 women were randomized to receive an intravaginal application of 5 g of 0.75% metronidazole gel, and another 112 women to receive placebo, administered prior to cesarean section. Eighty two per cent of women also received prophylactic cephalosporin after clamping of the cord.

MAIN OUTCOME MEASURES

Postcesarean endometritis (temperature ≥38°C on 2 postoperative days after the first day and one or more of uterine tenderness, tachycardia, foul-smelling vaginal discharge, or leukocytosis), other febrile morbidity, wound infection, length of hospital stay, neonatal outcomes.

MAIN RESULTS

Postpartum endometritis occurred in 7% of the metronidazole group, compared to 17% of the placebo group (p=0.02 ***, relative risk [RR] 0.4, 95% CI 0.2–0.9, number needed to treat to avoid one case of endometritis is 10, CI 5–74 **). There was no significant difference between groups in the rates of other maternal febrile morbidity (13 vs 19%, respectively) or wound infection (4 vs 3%). The mean length of postpartum stay was similar in the two groups (3.3 vs 3.5 days). The proportion of infants with Apgar score <7 at 5 min was 2% in the metronidazole group and 8% in the placebo group (p=0.03, RR 0.2, CI 0.1–0.9 **). There was no significant difference between groups in other neonatal outcomes, such as rate of cord pH <7.16 (9 vs 7%) or median length of hospital stay (3 days in both groups).

CONCLUSION

Intravaginal application of metronidazole gel prior to cesarean section reduced the risk of postpartum endometritis.
Commentary

Intraoperative antibiotic prophylaxis has been shown to reduce postcesarean section endometritis by about two-thirds. Previous studies of multiple antibiotic regimens have not proven them more efficacious than single antibiotic regimens. This well-designed trial is a welcome addition to the literature on this topic, because one of every five to six women who undergo cesarean section will have the complication, even with commonly used prophylactic regimens, such as first generation cephalosporins. Endometrial cultures from women with postpartum endometritis generally show mixed flora, including anaerobes such as *B. fragilis*. Treatment regimens for postpartum endometritis that include agents with good activity against such anaerobes have been shown to be superior to those without this activity. Although intravenous metronidazole with cephazolin has not been shown to be superior to cephazolin alone as intraoperative prophylaxis, the addition of intravaginal metronidazole to intravenous cephazolin is an approach that makes sense.

The design of this study was methodologically strong. It was randomized, double-blinded, placebo-controlled, and analyzed by intention-to-treat. The study size was large enough to detect a clinically significant difference in the principal outcome, diagnosis of postpartum endometritis. Importantly, there were no differences in distribution between study groups in variables that were likely to influence the rate of postpartum endometritis, such as elective vs emergency surgery, number of pelvic examinations, time elapsed from the first pelvic exam until delivery, and rupture of membranes on admission. Differences in other outcomes reported, such as length of postpartum hospital stay and low neonatal Apgar score and umbilical cord pH, may be more important to women and health care providers than the primary outcome studied here, and yet more difficult to detect. It would be worthwhile to determine what sample sizes would be required to establish whether differences in these secondary outcomes exist. It would also be worthwhile to study subgroups, such as women who meet Gram stain criteria to diagnose...
bacterial vaginosis, since they may be especially likely to benefit from the use of intravaginal metronidazole.

The use of adjunctive intravaginal metronidazole preoperatively resulted in a 10% absolute risk reduction for the prevention of postcesarean endometritis. The resulting number needed to treat to prevent one case of endometritis of 10 is quite favorable. The treatment is of low cost and relatively easy to administer. It is also unlikely to cause rare serious adverse effects that are difficult to document in trials of efficacy. This effective treatment should be adopted in clinical practice.

**Literature Cited**


*Numbers calculated from data in article.*