

Does Azithromycin Have a Role in Cesarean Sections?

Yes, adding azithromycin to the usual antibiotic protocol in nonelective c-sections reduces infections. But not everyone can take advantage of it.

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PRACTICE CHANGER

Prescribe a one-time dose of azithromycin (500 mg IV), along with standard antibiotic prophylaxis, at the time of cesarean delivery to prevent postoperative infections.

STRENGTH OF RECOMMENDATION

B: Based on a single, good-quality, randomized controlled trial.¹

A 26-year-old G1P0 at 40w1d presents in spontaneous labor and is dilated to 4 cm. The patient reached complete cervical dilation after artificial rupture of membranes and oxytocin augmentation. After four hours of pushing, there has been minimal descent of the fetal vertex beyond +1 station with significant caput succedaneum. Her physician decides to proceed with cesarean delivery.^{2,3} What antibiotics should be administered prior to incision to reduce postoperative infection?

The CDC reports that nearly 1.3 million cesarean deliveries were performed in the United States in 2015, which represents about a third of all births.⁴ C-section is the most common major surgical procedure performed in this country and is associated with an infection rate five to 10 times that of vaginal delivery.^{5,6} Pregnancy-associated infection, particularly during delivery, is a significant risk and the fourth most common cause of maternal death in the United States.⁵

The current standard of care in cesarean delivery is antibiotic prophylaxis (often a first-generation cephalosporin) prior to skin incision.⁷ The majority of c-sections performed are nonelective, and of these, postoperative infections occur in 12% of women who receive standard prophylaxis.^{8,9} A small, single-center design trial suggested that azithromycin adjunctive therapy expands antibiotic coverage to *Ureaplasma* species, resulting in a lower risk for postoperative infection.¹⁰

This study evaluated the use of azithromycin adjunctive therapy, in addition to standard antibiotic prophylaxis, to reduce the risk for postoperative infections in women receiving nonelective c-sections.

STUDY SUMMARY

Reduced infections up to 6 weeks post-c-section

A multicenter, randomized, double-blind trial conducted in 14 hospitals in the United States evaluated the effect of a one-time dose of azithromycin (500 mg IV) on post-cesarean infections. Women with a singleton pregnancy of at least 24 weeks' gestation were eligible for inclusion if they required



nonelective cesarean delivery during labor or at least four hours after membrane rupture. Patients were excluded if they had a known azithromycin allergy, subsequent vaginal delivery, azithromycin use within the week prior to randomization, extensive hepatic or renal dysfunction, a known history of prolonged QT interval, or substantial electrolyte abnormalities. Patients were eligible even if they were receiving other antibiotics for a positive group B *Streptococcus* screening.¹

All patients (N = 2,013) were treated with standard antibiotic prophylaxis (most often cefazolin), according to individual institution protocols. The women were randomized to receive either an azithromycin 500 mg/250 mL IV infusion (n = 1,019) or an identical placebo IV infusion (n = 994) within one hour of the procedure. The primary outcome was a composite endpoint of

endometritis, wound infection, or other infections occurring up to six weeks after the c-section. Secondary outcomes included neonatal death, sepsis, and other neonatal and maternal complications.¹

Patients in the placebo group had a higher rate of smoking during pregnancy; the researchers found no other significant differences.¹

Results. The primary composite outcome occurred less frequently in the azithromycin group than in the placebo group (6.1% vs 12.0%; relative risk [RR], 0.51; number needed to treat [NNT], 17). When the researchers looked at the individual elements of the primary composite outcome, two had significant reductions versus placebo. Endometritis (3.8% vs 6.1%; RR, 0.62; NNT, 43) and wound infections (2.4% vs 6.6%; RR, 0.35; NNT, 24) occurred significantly less frequently, but there was no difference for

other infections (0.3% vs 0.6%; RR, 0.49).

Serious maternal adverse events were also lower in the treatment group than in the control group (1.5% vs 2.9%; RR, 0.5; NNT, 71). There was no difference in composite secondary neonatal outcomes, including death and serious complications (14.3% vs 13.6%; RR, 1.05).¹

WHAT'S NEW

Fewer infections without more adverse events

This study showed that adding azithromycin to standard antibiotic prophylaxis within one hour of a c-section reduces post-cesarean delivery infection rates without increasing the risk for maternal or neonatal adverse events.

CAVEATS

Caution with prolonged QT

While azithromycin was efficacious and well tolerated in the study, not every patient can take it. Patients with a previous drug reaction or allergy should avoid it, and experts

ing fetal heart rate. In many of these cases, speed of cesarean delivery may mean the difference between positive and negative outcomes. Availability of azithromycin on labor and delivery floors for timely administration within one hour of the procedure is important.

Additionally, azithromycin has known QT prolongation risks.¹¹ While the baseline QT interval is not known for many healthy young women, this should be considered when azithromycin is utilized in combination with other medications that may prolong the QT interval. **CR**

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➤ Adding azithromycin to standard prophylaxis reduces infection rates without increasing adverse events.

advise prescribing it with caution for patients who have (or are at increased risk for) a prolonged QT interval, including those on other QT-prolonging medications.

Of note, women with scheduled c-sections and those with chorioamnionitis or another infection requiring postpartum antibiotics were excluded from this study. Thus, it is unknown if azithromycin use decreases complications in these patients.

CHALLENGES TO IMPLEMENTATION

Drug availability is key

Nonelective c-sections are performed based on many factors, including a nonreassur-