Published in final edited form as:

Am J Obstet Gynecol. 2018 April ; 218(4): 416.e1–416.e4. doi:10.1016/j.ajog.2018.01.016.

Applying surgical antimicrobial standards in cesarean deliveries

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Surgical site infections (SSIs) are the most common and cost-burdensome health care associated infections in the United States.¹ To prevent SSIs, preoperative administration of antibiotics with intraoperative redosing at 1e2 half-lives of the select agent or at an estimated blood loss (EBL) of 1500 mL is an established practice based on current guidelines for antimicrobial prophylaxis in surgery.² Yet in obstetric surgery, a single dose of preoperative antibiotics is considered standard of care in the United States.³ Although the principles for redosing antibiotics have been endorsed by the American College for Obstetricians and Gynecologists for gynecological procedures,⁴ no such recommendations have been made for obstetrical procedures.³

Failure to extend the standard of care to obstetrics is a recurrent shortcoming in the field, and obstetrical patients are routinely treated differently, in large part because of the exclusion of pregnant women from medical research.^{5–8} This shortcoming is apparent in open abdominal surgery. Redosing may be particularly important for the obstetrical population because of the increased rate of renal clearance in pregnancy and the associated unique pharmacokinetics of cefazolin at the time of delivery.⁹

Surgical guidelines for antimicrobial prophylaxis

Since 2013, the joint guidelines by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Surgical Infection Society, and the Society for Healthcare Epidemiology of America have described this common principle: “for all patients, intraoperative redosing is needed to ensure adequate serum and tissue concentrations of the antimicrobial if the duration of the procedure exceeds 2 half-lives of the drug or there is excessive blood loss during the procedure.”² This language contrasts with the same statement’s guidelines specifically for cesarean delivery: “additional intraoperative doses may be warranted for patients with excessive blood loss or for whom the duration of the procedure is extended.”²

This difference in language is also reflected in practice. At our institution, it is uncommon to redose antibiotics after an intraoperative postpartum hemorrhage, and in our review of the literature, we did not identify randomized trials or other studies of redosing in cesarean deliveries.

Risk of hemorrhage with cesarean delivery

Postpartum hemorrhage is defined as an estimated cumulative blood loss of 2:1000 mL accompanied by signs/symptoms of hypovolemia.¹⁰ According to data from the National Inpatient Sample compiled by the Centers for Disease Control and Prevention, the rate of postpartum hemorrhage per 10,000 deliveries has increased from 4.3 in 1993 to 21.2 in 2014, perhaps related to contemporaneous trends in advancing maternal age, abnormal placentation, obesity, and multifetal gestations.^{11–13}

Although the use of adjunct measurements such as the shock index and hemorrhage protocols requiring direct calculation of blood loss have improved recognition of hemorrhage, precise estimation of blood loss at the time of cesarean delivery remains challenging.^{14,15} Through quantification based on pre- and postdelivery hematocrit, data suggest that 18% and 10% of primary and repeat cesarean deliveries, respectively, have a calculated blood loss of greater than 1500 mL.¹⁶

Data supporting antibiotic redosing

Available data do support the redosing parameters utilized in surgery today. First, pharmacokinetic studies have found cefazolin concentration below minimum inhibitory concentrations for common pathogens in patients' serum and tissue 3 hours after dosing.^{17,18} Redosing at an EBL of 1500 mL is also supported by the pharmacokinetic data that demonstrated that tissue cefazolin concentration is inversely related to blood loss.¹⁹ Similar findings have been reported when the volume of replacement fluids served as an indicator of blood loss.²⁰

Second, there have been a number of clinical observational and interventional studies supporting the significance of redosing as well.^{21–24} A prospective, observational, multicenter study of 4472 cardiac, arthroplasty, and hysterectomy cases found greater than 3 times the risk of SSIs among those who did not receive redosing.²⁵

One randomized controlled trial (RCT) of patients undergoing elective colorectal surgery did not demonstrate a significant difference between patients who received a single dose vs those who were redosed 2 hours after the surgery began.²⁶ However, in this study, in the subset of procedures lasting longer than 3 hours, there was a statistically significantly greater number of infections, adding to the notion that both time and blood loss contribute to decreased efficacy of single-dose antimicrobial prophylaxis. Current professional society guidelines advise redosing antibiotics based on these data that are available.

Current investigations for antimicrobial strategy during cesarean deliveries

In obstetrics, a major current focus regarding antimicrobial prophylaxis is the addition of extended spectrum antibiotics to the routine use of cefazolin. An RCT comparing preoperative cefazolin to cefazolin with azithromycin recently demonstrated significant reduction in infectious surgical complications among women undergoing nonelective cesarean deliveries, with no difference in adverse neonatal outcomes.²⁷ However, there are concerns about promoting antibacterial resistance via the use of an additional parenteral

agent with broad-spectrum activity, and its routine use is not yet endorsed by the American College for Obstetricians and Gynecologists.

The use of oral cephalexin and metronidazole following cesarean delivery to reduce SSIs was recently evaluated in an RCT, which demonstrated a significant decrease in infection risk within the study population of obese women at a single institution.²⁸ There were no serious maternal adverse events, but other maternal and neonatal adverse effects as well as societal costs are not known.²⁹

Conclusion

It is unclear why redosing is not practiced in obstetrics. Indeed, it is more likely that a woman's surgical team will experience an EBL >1500 mL in a cesarean delivery than in a hysterectomy.^{16,30} Therefore, it is logical and necessary to apply infection risk reduction strategies from general surgery, already being utilized in gynecological procedures with similar clean-contaminated designations, to obstetrical surgery. The platform to integrate redosing into practice at the time of cesarean delivery already exists because most institutions have well-designed hemorrhage protocols with time-outs at specific blood loss levels.

Not every decision in medicine can be based on gold standard study designs. Furthermore, an RCT on this topic would be logistically challenging because all patients admitted for delivery would need to be approached, given that it would not be possible to obtain consent at the time of a qualifying hemorrhage, and costly, given the large number of participants required. Yet there is a large and growing need to improve antimicrobial prophylaxis within this obstetrical cohort.

Ideally, a regimen that is efficacious, cost effective, and safe with minimal risk of contributing to antibiotic resistance should be utilized. While additional research in this field is needed, we propose that adopting the practices of the other surgical specialties by redosing at either an EBL of 1500 mL or a prolonged operation represents an opportunity to further reduce infectious complications in this subset of women at increased risk of SSIs. This practice is now endorsed by select institutions in the United States and the Society of Obstetricians and Gynaecologists of Canada.³¹

The momentum in obstetrics may be moving primarily toward the utilization of broader-spectrum antibiotics, yet redosing offers a simpler intervention, with known safety and cost profiles, in the effort to reduce cesarean morbidity.

Acknowledgments

We thank Dr Michael Socol for comments that greatly helped to improve the manuscript.

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