Antimicrobial Prophylaxis of Cesarean Section

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The letter to the editor in this issue[1] responds to an earlier letter by Dougherty and Williams.[2] These correspondences require some editorial comments regarding the use of antimicrobials for minimizing infectious morbidity following cesarean sections. Numerous publications, including the *Medical Letter*,[3] have advocated the application of antimicrobial infusions upon clamping the umbilical cord following a cesarean section delivery. Various drugs have been successfully used for this purpose, including older penicillins (ampicillin) and cephalosporins of all generations.[4-7] Occasionally, a statistically valid difference has been observed between regimens, but a concensus of all publications would not substantiate a clear advantage of one drug regimen over another. Cost differences, however, do exist.

Cephalosporins developed in the last decade have been more expensive to use for surgical prophylaxis and have rarely proven advantageous compared to previously used drugs in "multiple dose" comparison trials. This fact led the pharmaceutical manufacturers to explore the new compounds in "cost-effective" single dose or short course regimens for prophylaxis of most types of surgical procedures. In single dose trials, these newer antimicrobial agents have shown clinical equality to drug package insert schedules (multiple doses) for cefazolin or cefoxitin, leading to Federal Drug Administration (FDA&approved indications. In contrast, the FDA-approved indications for single dose prophylaxis with "first generation" or the older "second generation" cephalosporins have been slow to emerge. These observations apply to cesarean section prophylaxis. Futhermore, a single dose cefazolin regimen recently was associated with a significantly ($p<.05$) higher rate of endomyometritis compared to the multiple dose cefazolin regimen for cesarean sections (R. Sweet, personal communication, 1990)

Relevant to the issues cited in the letters, two cefoxitin-like cephamycin agents are now clinically available. Cefmetazole and cefotetan have both demonstrated acceptable clinical efficacy used for cesarean section prophylaxis.[8-10] In fact, in some studies (including personal observations) the newer compounds appear to have lower rates of postoperative infectious complications.[10,11] The balanced spectrums of activity provided by cefoxitin, cefmetazole and cefotetan are very similar against the significant female genital tract pathogens.[12,13] Thus, it seems illogical to blame only one of these drugs (and not all) as being at fault in producing increased rates of postcesarean infection.[2] The cited responses of the complication cases to cefotetan plus gentamicin treatment[2] would imply that cefotetan lacks a gram-negative aerobic spectrum sufficient to prevent the infection. Morever, subsequent prophylaxis with cefoxitin resulted in the return to low complication rates.[2] A critical review of the documented cefotetan and cefoxitin spectrums would show that cefotetan is actually superior to cefoxitin against the suspected pathogens.[14,15] In most comparisons, cefotetan may cover as much as 20% more enteric bacilli than cefoxitin.[16]

Investigators reporting prophylaxis studies and epidemiologic data should be very cautious in their analyses.[2] Because large numbers of evaluable patient cases are required to prove statistical differences between prophylaxis drugs, studies with less than 1,000 randomized patients rarely demonstrate a superiority of one regimen in the absence of experimental or interpretive error. Indeed, epidemic transient variations in the postoperative infection rates do occur.[1,2] These changes are more

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likely the results of procedural variations or factors other than the more easily controlled prophylactic drug.

In conclusion, a wide variety of safe β-lactams can be used with confidence for cesarean section prophylaxis. If antimicrobial resistance were a valid concern, the most cost-effective single-dose regimens[3] would be of little value because cefazolin-like cephalosporins have a more compromised spectrum compared to "second generation" cephamycins,[14,15] "third generation" cephalosporins[17] or the β-lactamase inhibitor combinations.[18] Complicating our understanding has been the lack of FDA-approved cesarean section prophylaxis indications for single doses of cefazolin (1 g) or ampicillin (1 g or 2 g) while newer, broad-spectrum drugs have the potency and indications for this procedure. In response to Dougherty's and Williams' title question "Prophylaxis of Cesarean Section-Where to Turn?" I believe that current ethical medical practice offers many study-proven valid and cost-effective single dose alternatives. The choice actually seems to be between single dose FDA-indicated drugs and those older compounds that are most effective as multiple dose schedules. It's time for surgeons, epidemiologists and infectious disease experts to recognize the equality of numerous β-lactams for the prophylaxis of cesarean section and other obstetrical and gynecologic procedures.

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