TITLE: Antibiotics for the Prevention of Post-Cesarean Section Complications: Clinical Evidence and Safety

DATE: 07 February 2013

RESEARCH QUESTIONS

1. What is the clinical evidence regarding the effectiveness and safety of antibiotic prophylaxis administered before or after clamping during cesarean sections for the prevention of maternal post-surgical infections?

2. What is the clinical evidence regarding the effects of antibiotic prophylaxis administered before or after clamping during cesarean section on neonatal health and antibiotic resistance?

KEY MESSAGE

Four systematic reviews and meta-analyses, four randomized controlled trials, and five non-randomized studies were identified regarding the timing of antibiotic administration for the prevention of post-cesarean section maternal and neonatal complications.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2012, Issue 12), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between Jan 1, 2008 and Jan 23, 2013. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.
RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and non-randomized studies.

Four systematic reviews and meta-analyses, four randomized controlled trials, and five non-randomized studies were identified regarding the timing of antibiotic administration for the prevention of post-ceesarean section maternal and neonatal complications. No relevant health technology assessment reports were identified. Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

Maternal Health
All of the included studies examined the effect of antibiotic administration on maternal health.1-13 Evidence from one systematic review2 and one non-randomized study11 suggested that compared to no antibiotic prophylaxis, antibiotic administration was beneficial in reducing post cesarean section infectious complications. With respect to the timing of prophylaxis, the evidence was mixed. The authors of two systematic reviews1,4 and four non-randomized studies9,10,12,13 found differences in rates of infections and concluded that pre-operative antibiotic administration reduced rates of post-cesarean section complications1,4,10 and recommended pre-operative antibiotic administration.9,12,13 The authors of one systematic review3 and four randomized trials5-8 found that the administration of antibiotics was effective in reducing infectious complications following cesarean section, but that the timing of administration was not a factor in reducing infections. The authors of one study recommended that for elective cesarean section, antibiotics should be used after clamping, but that for non-elective cesarean section they should be used prior to incision.7

Neonatal Health
The majority of the included studies were either underpowered to detect neonatal events1,2 or did not examine the effects of the antibiotics on neonatal health.3,6,10,11,13 The studies that did examine neonatal events found that antibiotics, administered either before skin incision or after cord clamping, had no effect on neonatal outcomes following cesarean section.4,5,7-9,12 Further study regarding neonatal outcomes was recommended.2,3

Antibiotic Resistance
Little information was identified regarding antibiotic resistance. Methicillin-resistant Staphylococcus aureus was the most common organism found in maternal wound infections in one study10 and further study was recommended by the authors of that study, as well as the authors of one of the included systematic reviews.3

Further detail regarding the included studies is provided in Table 1.
### Table 1: Summary of Included Studies

<table>
<thead>
<tr>
<th>Author, Date</th>
<th>Study Objectives</th>
<th>Results</th>
<th>Conclusions</th>
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<tbody>
<tr>
<td><strong>Systematic Reviews and Meta-Analyses</strong></td>
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<td>Baaqeel &amp; Baaqeel, 2012&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Compare the rates of maternal and neonatal infections when antibiotics are administered either preoperatively or after cord clamping.</td>
<td>Pre-operative administration was associated with a 41% reduction in endometritis compared to administration after cord clamping. There were non-significant reductions: in wound infections, maternal febrile morbidity, neonatal sepsis, and NICU admission.</td>
<td>Pre-operative administration of antibiotics significantly reduced the rate of endometritis following c-section. There was limited power to detect neonatal events.</td>
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<td>Smaill &amp; Gyte, 2010&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Assess the effects of antibiotics versus no antibiotic prophylaxis on infectious morbidity in women undergoing c-section.</td>
<td>Antibiotic prophylaxis resulted in substantial reductions in fevers, wound infections, endometritis, serious infections, and infection-related complications. There were no reports of neonatal complications, however thrush was not assessed. Results were similar for administration before or after cord clamping.</td>
<td>Antibiotic prophylaxis for women undergoing c-section was found to be beneficial for maternal health, however there was no certainty regarding neonatal events.</td>
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<td>Tita et al., 2009&lt;sup&gt;3&lt;/sup&gt;</td>
<td>To examine different strategies for antibiotic prophylaxis for the prevention of infections in women undergoing c-section.</td>
<td>The use of pre-operative cefazolin administration and the use of extended spectrum antibiotics (with azithromycin or metronidazole) after cord clamping resulted in up to a 50% reduction in maternal infections. Studies comparing the two strategies were not identified.</td>
<td>Both antibiotic regimens were found to be effective in reducing maternal infections. Future studies examining neonatal outcomes and antibiotic resistance were suggested.</td>
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<td>Constantine et al., 2008&lt;sup&gt;4&lt;/sup&gt;</td>
<td>To examine the effects of timing of antibiotic prophylaxis during c-section.</td>
<td>Pre-operative administration of antibiotics significantly reduced the risk of post-partum endometritis and the total number of maternal infections. There was a trend toward lower incidence of wound infections. Pre-operative administration had no effect on neonatal sepsis (suspected or confirmed) or on admissions to the NICU.</td>
<td>Antibiotic administration prior to incision resulted in lower risk of endometritis and infections without having negative neonatal outcomes.</td>
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<td><strong>Randomized Controlled Trials</strong></td>
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<td>Macones et al., 2012&lt;sup&gt;5&lt;/sup&gt;</td>
<td>To compare the effects of antibiotics administered either prior to incision or after cord clamping on both maternal and neonatal health.</td>
<td>The timing of antibiotic administration resulted in no difference in a composite of maternal infectious morbidity (postoperative fever, wound infection, endometritis, urinary tract infection). Neonatal outcomes were similar in both groups.</td>
<td>The authors concluded that both pre-operative and post-clamping administration of antibiotics were reasonable regimens for the prevention of post-c-section complications.</td>
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<td>Witt et al., 2011&lt;sup&gt;6&lt;/sup&gt;</td>
<td>To compare the effectiveness of cefazolin administered pre-</td>
<td>There were no statistically significant differences between pre-operative administration and post-clamping administration in maternal infectious</td>
<td>Authors concluded that while the timing of cefazolin administration was not important,</td>
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<td>operatively, post-clamping, or placebo for the prevention of post-c-section complications</td>
<td>morbidity following elective c-section.</td>
<td>antibiotics were more effective than placebo at preventing infectious morbidity following elective c-section.</td>
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<td>Nokiani et al., 2009⁷</td>
<td>To compare the effectiveness of cefazolin administered pre-operatively or post-clamping for the prevention of post-c-section complications.</td>
<td>There were no significant differences between the two groups with respect to neonatal complications.</td>
<td>Authors recommended that for elective c-section, cefazolin should be used after clamping but that for non-elective c-sections, it should be used prior to incision.</td>
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<td>Yildirim et al., 2009⁸</td>
<td>To determine whether the timing of antibiotic prophylaxis has an effect on maternal and neonatal outcomes following c-section.</td>
<td>There were no significant differences found between groups regarding total infectious morbidity or endometritis and no increases in neonatal sepsis, sepsis workup, need for neonatal intensive care, or intensive care stay.</td>
<td>Authors concluded that the timing of antibiotic prophylaxis did not affect maternal or neonatal outcomes.</td>
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<td>Brown et al., 2013⁹</td>
<td>To evaluate the differences in post-c-section complications before and after a policy change regarding the timing of antibiotic prophylaxis.</td>
<td>There rates of post-c-section complications dropped from 10.8% to 2.8% in the year following the policy change from antibiotic administration after cord clamping, to administration prior to incision, with no difference in adverse events on neonates.</td>
<td>Authors concluded that antibiotics should be given prior to incision in Australia and New Zealand.</td>
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<td>Thurman et al., 2010¹⁰</td>
<td>To compare post-c-section infection rates before and after the implementation of a preoperative antibiotic administration policy.</td>
<td>After the policy implementation, the rates of post-c-section infectious complications decreased from 20.7% to 8.5%. MRSA was the most common organism present in wound infections.</td>
<td>Authors recommended further study regarding optimal antibiotic regimens and antibiotic resistance.</td>
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<td>Dinsmoor et al., 2009¹¹</td>
<td>To examine the efficacy of antibiotic administration in non-labouring women undergoing c-section.</td>
<td>Antibiotic administration was associated with lower rates of endometritis (2.0% vs. 2.6%) and wound infection (0.52% vs. 0.96%) versus no antibiotics.</td>
<td>Authors concluded that antibiotic administration significantly reduced the rates of endometritis and wound infections in non-labouring women undergoing c-section.</td>
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<td>Owens et al., 2009¹²</td>
<td>To examine the effects of a change in the timing of antibiotic administration for the prevention of post-c-section complications.</td>
<td>Pre-incision administration resulted in lower rates of endometritis (2.2% vs. 3.9%) and wound infection (2.5% vs. 3.6%) compared with administration following cord clamping without having any negative effects on neonatal infection rates or health.</td>
<td>Authors concluded that antibiotic administration should occur prior to skin incision.</td>
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<td>Kaimal et al., 2008¹³</td>
<td>To examine the effect of a policy change in SSI rates fell from 6.4% (post-cord clamp administration) to 2.5% (pre-</td>
<td></td>
<td>Authors concluded that antibiotic administration</td>
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<td>the timing of antibiotic prophylaxis for the prevention of post-c-section SSIs.</td>
<td>incision administration). There was also a decrease in the rates of endometritis and a trend toward decreased cellulitis.</td>
<td>prior to c-section incision lead to a significant decrease in SSIs.</td>
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</table>

c-section = cesarean section; MRSA = methicillin-resistant *Staphylococcus aureus*; NICU = neonatal intensive care unit; SSI = surgical site infections; vs = versus
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses


Randomized Controlled Trials


Non-Randomized Studies


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APPENDIX – FURTHER INFORMATION:

Guidelines and Recommendations


Surveys of Clinical Practice


Review Articles


Additional References


21. Lyimo FM, Massinde AN, Kidonya BR, Konje E, Mshana SE. Efficacy of single dose of gentamicin in combination with metronidazole versus multiple doses for prevention of post-caesarean infection: study protocol for a randomized controlled trial. Trials [Internet].