Efficacy and safety of broad spectrum penicillins with or without beta-lactamase inhibitors versus 1st and 2nd generation cephalosporins as prophylactic antibiotics at cesarean section: a systematic review and meta-analysis

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Research Article

Keywords: caesarean section, cephalosporins, broad spectrum penicillins, beta-lactamase inhibitors, postoperative infection

Posted Date: August 26th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1980049/v1

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Abstract

**Purpose** To assess the efficacy and safety between broad spectrum penicillins with or without beta-lactamase inhibitors versus 1st and 2nd generation cephalosporins in prevention of post-caesarean infections.

**Methods** Randomized controlled trials (RCTs) comparing broad spectrum penicillins with or without beta-lactamase inhibitors to 1st and 2nd generation cephalosporins were searched in foreign databases, such as the Cochrane Library, PubMed and EMBASE, and chinese databases, including the China National Knowledge Infrastructure (CNKI) WanFang Data and China Science and Technology Journal Database(CSTJ). The included RCTs were analyzed by the software Rev Man 5.4.

**Results** A total of nine RCTs, 1998 patients were involved. Six trials compared broad spectrum penicillins plus beta-lactamase inhibitors versus 1st and 2nd generation cephalosporins, we found there were no differences between interventions for endometritis (RR 0.85, 95% CI 0.57–1.26, $I^2 = 0.0\%$), wound infection (RR 1.28, 95% CI 0.53–3.12, $I^2 = 0.0\%$), urinary tract infection (RR 1.70, 95% CI 0.06–47.34, $I^2 = 79\%$), febrile morbidity (RR 0.95, 95% CI 0.32–2.84, 1 study), maternal rashes (RR 1.20, 95% CI 0.26–5.58, $I^2 = 0.0\%$). Four trials compared broad spectrum penicillins versus 1st and 2nd generation cephalosporins, we found there were no differences between interventions for endometritis (RR 3.22, 95% CI 0.45–22.89, $I^2 = 64\%$), febrile morbidity (RR 1.93, 95% CI 0.48–7.83, $I^2 = 84\%$), wound infection (RR 1.19, 95% CI 0.20–6.97, $I^2 = 70\%$), urinary tract infection (RR 9.00, 95% CI 0.49–163.90, 1 study). The postoperative length of stay was longer for women in the broad spectrum penicillins group than 1st generation cephalosporins group (MD 1.50, 95% CI 0.54–2.46, 1 study).

**Conclusion** Based on the results of this study, broad spectrum penicillins with or without beta-lactamase inhibitors and 1st and 2nd generation cephalosporins may have similar efficacy at caesarean section regarding postoperative infections. PROSPERO Registration Number: CRD42022345721.

Introduction

Cesarean section is a routine and important operation to solve critical cases in obstetrics. With the development of cesarean section, the rate of cesarean delivery is increasing all over the world[1]. However, Cesarean section is considered to be a clean-contaminated procedure that is one of the most important risk factors for postpartum infection, with a global infection range of 2.5–20.5%[2], and the risk of infections is 5–20 times higher for women who have a cesarean delivery than vaginal births[3]. Good surgical technique is important to reduce infections, additionally, guideline of American College of Obstetricians and Gynecologists(ACOG)[4] recommends that the use of prophylactic antibiotic before cesarean section can reduce postoperative endometritis, wound infection, fever, and severe infectious complications such as pelvic abscess, bacteremia, sepsis, etc., these more serious complications can lead to maternal deaths. Common use of prophylactic antibiotics decrease the risk of these postoperative infections by more than 50%[5]. In addition, antibiotics can cause adverse effects in the mother and infant. Antibiotics administered to women at the time of delivery may exert a direct impact on the offspring's microbiota and interfere with the development of the infant's immune system[6]. Therefore, the selection of effective and safe prophylactic antibiotics is particularly important.
Prophylactic antibiotics at cesarean section should be effective against the following pathogens: the main causative agents are skin colonizers, primarily gram-positive cocci, particularly including Staphylococcus aureus and Streptococci; vaginal colonizers, including anaerobes and, gram-negative bacilli[7]. Furthermore, such a ideally prophylactic antibiotics should be[8]: (1) Not related to the development of antimicrobial resistance, (2) Able to attain adequate serum and tissue levels throughout the procedure, (3) Less over-priced and well-tolerated. At present, The guideline for clinical application of antimicrobial therapy in china recommends the 1st and 2nd generation cephalosporins with or without metronidazole as prophylactic antibiotics[9]. The ACOG[4] and the Canadian Society of Obstetrics and Gynaecology[8] have recommended 1st generation cephalosporins such as cefazolin as first choice for prophylaxis. In spite of there are clear guidelines regarding recommendation of prophylactic antibiotics, differences in clinical practices remain, which is interfered by many factors, depending on patient’s particular condition or obstetricians’ preference. Several clinical studies[7] have also reported the use of broad-spectrum penicillins or penicillins plus betalactamase inhibitors (e.g. Ampicillin and Ampicillin/sulbactam) as prophylaxis. Although broad-spectrum penicillins are similar in antibacterial spectrum to 1st and 2nd generation cephalosporins, the use of broad-spectrum penicillins as antibiotic prophylaxis remains questionable, considering that ampicillin is prone to produce resistant enzymes to staphylococcus, resulting in ineffectiveness against Staphylococcus, and allergic reactions to penicillins under anesthesia are difficult to identify[10]. Compared with the 1st and 2nd generation cephalosporins, the antimicrobial combination of ampicillin/sulbactam has broader antibacterial spectrum including anaerobic bacteria and Enterococci[11]. This study mainly assessed the efficacy and safety of the broad-spectrum penicillins (P2) with and without beta-lactamase inhibitors (P2+) versus 1st and 2nd generation cephalosporins (C1&C2) in reducing postoperative infections for women and adverse effects on mother and infant.

Methods

The protocol for this review was registered in the PROSPERO International Prospective Register of Systematic Reviews (CRD42022345721). We selected RCTs by retrieving foreign medical databases (Cochrane Library, PubMed and Embase) and domestic databases (CNKI, CSTJ, Wanfang Data). The English search terms included “Ampicillin”, “Cefazolin”, “Cefuroxime”, “Cephalosporins”, “Cesarean section”, etc.. The Chinese search terms were “Anbianxilin”, “Toubaozuoling”, “Toubaojunsu”, “Pougongchan”, etc.. The database was collected up to Jan, 2022. In addition, we manually screened references of studies and review articles for relevant articles.

Inclusion criteria: (1) Type of study: RCTs; (2) Subjects: pregnant women undergoing caesarean section, both elective and non-elective.

Exclusion criteria

(1) Non-RCTs; (2) patients with inconsistent baseline data and; (3) reports were incomplete, outcome effects were unclear or unable to extract data for analysis.

Intervention: (1) The comparison of broad-spectrum penicillins plus beta-lactamase inhibitors versus 1st and 2nd generation cephalosporins; (2) The comparison of broad-spectrum penicillins versus 1st and 2nd
generation cephalosporins.

**Main outcomes**

endometritis, febrile morbidity, wound infection, urinary tract infection, maternal rashes, length of hospital stay.

Two investigators independently selected the literatures according to the pre-established inclusion and exclusion criteria, carried out data extraction and assessed risk of bias for each study using the criteria outlined in the Cochrane Handbook.

The meta-analysis was performed using Rev Man 5.4 software. The enumeration data of outcome evaluation were statistically analyzed using the relative risk (RR). The continuous data were analyzed using mean difference (MD). The 95% confidence interval (95% CI) was used for interval estimation. Heterogeneity was assessed using the $I^2$ test. If $I^2 < 50\%$, the fixed-effect model was used. If $I^2 > 50\%$, it indicated that there was statistical heterogeneity between trials. If there was no clinical or methodological heterogeneity, the random-effect model was preferred.

**Result**

**Search results**

The database search with appropriate search strategy, including English and Chinese databases, retrieved 418 records. A total of 243 studies were retained after duplicates were removed, then 225 studies were excluded because the title/abstract did not meet the inclusion criteria or satisfied one of the exclusion criteria. After reading the full text, 9 articles were excluded. The last 9 RCTs were included (Fig.1).

**Included studies characteristics**

A total of nine RCTs involving 1998 pregnant women were eligible in the meta-analysis. Six studies compared broad-spectrum penicillins plus beta-lactamase inhibitors versus 1st and 2nd generation cephalosporins[12-17], four studies compared broad-spectrum penicillins to 1st and 2nd generation cephalosporins[14,18-20]. Characteristics of the nine included studies are shown in Table 1.

**Risk of bias assessment**

Among the nine studies, three [12,14,15] were randomized double-blind studies and two [16,18] were randomized single-blind study, and four[13,17,19,20] were described as RCTs. We assessed included studies for risk of bias followed the methods described in the Cochrane Handbook. Risk of bias of eligible studies presents in Figs. 2 and 3.
<table>
<thead>
<tr>
<th>Study</th>
<th>Type of study</th>
<th>Number of participants</th>
<th>Intervention</th>
<th>Dose and timing of administration</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bracero 1997[12]</td>
<td>Double-blind RCT</td>
<td>170</td>
<td>Ampicillin/sulbactam 1.5g, Cefotetan 1g</td>
<td>single dose, IV, at time of umbilical cord clamping</td>
<td>Endometritis; Wound infection; Urinary tract infection; Febrile morbidity; Maternal rashes</td>
</tr>
<tr>
<td>Noyes 1998[13]</td>
<td>RCT</td>
<td>292</td>
<td>Ampicillin/sulbactam 1.5g, Cefazolin 1g, Cefotetan 1g</td>
<td>single dose, IV, after umbilical cord clamping</td>
<td>Endometritis; Maternal rashes</td>
</tr>
<tr>
<td>Spinnato 2000[14]</td>
<td>Double-blind RCT</td>
<td>298</td>
<td>Ampicillin/sulbactam 3g, Ampicillin 2g, Cefotetan 2g</td>
<td>single dose, IV, after umbilical cord clamping</td>
<td>Endometritis</td>
</tr>
<tr>
<td>Busowski 2000[15]</td>
<td>Double-blind RCT</td>
<td>75</td>
<td>Ampicillin/sulbactam 1.5g, Cefotetan 1g</td>
<td>single dose, IV, after umbilical cord clamping</td>
<td>Endometritis; Wound infection; Urinary tract infection</td>
</tr>
<tr>
<td>Ziqgos 2010[16]</td>
<td>Single-blind RCT</td>
<td>176</td>
<td>Ampicillin/sulbactam 3g, Cefuroxime 1.5g</td>
<td>Single dose, IV, after umbilical cord clamping</td>
<td>Wound infection; Endometritis</td>
</tr>
<tr>
<td>Jyothi 2010[17]</td>
<td>RCT</td>
<td>122</td>
<td>Amoxycillin-clavulanic acid 2.4g, Cefazolin 2g</td>
<td>single dose, IV, after umbilical cord clamping</td>
<td>Endometritis; Wound infection</td>
</tr>
<tr>
<td>Mivumbi 2014[18]</td>
<td>Single-blind RCT</td>
<td>132</td>
<td>Ampicillin 2g, Cefazolin 1g</td>
<td>Single dose, IV, no more than 60 minutes prior to skin incision.</td>
<td>Endometritis; Wound infection; Urinary tract infection; Length of postoperative stay</td>
</tr>
<tr>
<td>Zhang 2010[19]</td>
<td>RCT</td>
<td>673</td>
<td>Ampicillin 2g, Cefazolin 1g</td>
<td>Multiple-day regimen, IV, no more than 60 minutes prior to skin incision, after surgery immediately, and 6 hours after surgery</td>
<td>Febrile morbidity; Wound infection</td>
</tr>
<tr>
<td>Study</td>
<td>Type of study</td>
<td>Number of participants</td>
<td>Intervention</td>
<td>Dose and timing of administration</td>
<td>Outcomes</td>
</tr>
<tr>
<td>---------------</td>
<td>---------------</td>
<td>------------------------</td>
<td>---------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Fang2021[20]</td>
<td>RCT</td>
<td>60</td>
<td>Ampicillin 2g</td>
<td>Single dose, IV, no more than 60 minutes prior to skin incision.</td>
<td>Wound infection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cefuroxime 1.5g</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Main outcomes

P2+ versus C1&C2-Outcome1: endometritis

The endometritis was reported in 6 studies[12-17] involving 1032 women were included in the meta-analysis. There was no significant difference between groups for post-caesarean endometritis(RR 0.85, 95% CI 0.57-1.26, $I^2$=0.0%) (Fig.4).

P2+ versus C1&C2-Outcome2: wound infection

The wound infection was reported in 4 studies[12,15-17] involving 543 women were included in the meta-analysis. There was no evident difference between groups concerning postoperative wound infection(RR 1.28, 95% CI 0.53-3.12, $I^2$=0.0%) (Fig.5).

P2+ versus C1&C2-Outcome3: urinary tract infection

The urinary tract infection was reported in 2 studies[12,15] involving 245 women were included in the meta-analysis. There was no clear difference in postoperative urinary tract infection between groups(RR 1.70, 95% CI 0.06-47.34, $I^2$=79%) (Fig.6).

P2+ versus C1&C2-Outcome4: febrile morbidity

Only one RCT[12]reported the incidence of febrile morbidity in pregnant women. There was no important difference between groups regarding post-caesarean febrile morbidity(RR 0.95, 95% CI 0.32-2.84).

P2+ versus C1&C2-Outcome5: maternal rashes

The maternal rashes was reported in two studies[12,13] involving 462 women were included in the meta-analysis. There was no significant difference for postpartum rashes between broad spectrum penicillins plus beta-lactamase inhibitors and 1st and 2nd generation cephalosporins(RR 1.20, 95% CI 0.26-5.58, $I^2$=0.0%) (Fig.7).

P2 versus C1&C2-Outcome1: endometritis

The endometritis was reported in two studies[14,18] involving 329 women were included in the meta-analysis. There was no significant difference between groups concerning post-caesarean postoperative endometritis(RR 3.22, 95% CI 0.45-22.89, $I^2$=64%) (Fig.8).
P2 versus C1&C2-Outcome2: wound infection

The wound infection was reported in three studies[18,19,20] involving 647 women were included in the meta-analysis. There was no evident difference in postoperative wound infection between groups (RR 1.19, 95% CI 0.20-6.97, $I^2=70\%$) (Fig.9). Due to the heterogeneity, subgroup analyses were carried out according to the subclasses of cephalosporins, region, dosage regimen(Fig.10).

P2 versus C1&C2-Outcome3: febrile morbidity

The febrile morbidity was reported in two studies[18,19] involving 329 women were included in the meta-analysis. There was no evident difference between groups for postoperative febrile morbidity(RR 1.93, 95% CI 0.48-7.83, $I^2=84\%$) (Fig.12).

P2 versus C1&C2-Outcome4: urinary tract infection

Only one RCT[18] reported the incidence of urinary tract infection in pregnant women. There was no important difference between groups in postoperative urinary tract infection(RR 9.00, 95% CI 0.49-163.90).

P2 versus C1&C2-Outcome5: length of postoperative stay

Only one RCT[18] reported length of postoperative stay in pregnant women. A increase was observed regarding length of postoperative stay in women who received broad spectrum penicillins to 1st generation cephalosporins (MD 1.50, 95% CI 0.54-2.46).

Discussion

During cesarean section, causative agents that colonize the vagina and cervix may transferred into the uterine cavity. Postoperative uterine tissue trauma, bleeding, exudate are also conducive to the generation of pathogens. Additionally, the surgical procedure changes the normal bacterial flora of the genital tract, resulting in the imbalance of the ratio of anaerobes to aerobes, which is easy to cause maternal infections when the postoperative immunity is decreased. So, the use of prophylactic antibiotics is recommended for all patients undergoing cesarean section. Clinical research practice has indicated[3] that there is no significant difference between 1st and 2nd generation cephalosporins in reducing the post-caesarean infections, and a single dose regimen is usually recommended.

The most common pathogens isolated from wound infection included Ureaplasma, Staphylococcus and Enterococcus[21] that can contaminate the myometrium, uterine blood vessels and lymphatic vessels, leading to infections such as endometritis during surgery. 1st and 2nd cephalosporins have been widely used as a preventive measure in obstetrics and gynecology surgery. However, they are naturally resistant to Enterococcus but stable to the beta-lactamase produced by Staphylococci[22]. It has been reported that Enterococcus are most common pathogens in cases of endometritis following cephalosporins prophylaxis[23]. Compared with 1st and 2nd cephalosporins, broad-spectrum penicillins is effective against Enterococcus and similar against negative bacteria, but not against Staphylococci. Broad-spectrum penicillins plus beta-lactamase inhibitors have a broader antimicrobial spectrum than 1st and 2nd
cephalosporins and are active against gram-positive, gram-negative and anaerobic bacteria, including S. aureus, Enterococci, Streptococci, many Enterobacterales and bacteroides spp. The aim of the present analysis was to evaluate the efficacy of broad-spectrum penicillins with or without beta-lactamase inhibitors which are routinely used clinically versus the 1st and 2nd generation cephalosporins which are the first choices as prophylactic antibiotics at cesarean delivery.

Cesarean section is the most important risk factor for postpartum endometritis[24]. Postoperative endometritis reported in 40–70% of patients before prophylactic antibiotic therapy became standard practice, especially in pregnant women with high risk factors of infection, such as rupture of membranes, excessive vaginal examinations before cesarean section, maternal anaemia as well as poor hygiene. The use of prophylactic antibiotics reduced the incidence of endometritis by 50%[25,26]. In addition, bacterial vaginosis result in high concentrations of pathogenic anaerobe, which is also associated with postpartum endometritis [27]. The results showed that there was no significant differences between broad-spectrum penicillins with or without beta-lactamase inhibitors and 1st and 2nd generation cephalosporins for postoperative endometritis. In terms of the comparison of broad-spectrum penicillins versus 1st and 2nd generation cephalosporins, however, our results were inconsistent with a review by Cochrane [28], which indicated that broad-spectrum penicillins were more effective than cephalosporins in preventing post-caesarean endometritis(RR 2.18, 95% CI 1.30 to 3.66). The source of difference may be the inclusion of a latest RCT[18], which reported a significant difference in the incidence of endometritis between the ampicillin and the cefazolin (15.2% vs 1.5%; P = 0.009), cephalosporins had more effective in the prevention of endometritis.

Wound infection refers to infection of the skin and subcutaneous tissue at the surgical site that can complicate cesarean section[29]. In addition, wound infection at the surgical site will result in therapeutic antibiotic use, further hospital stay, hospitalization costs and readmission costs[30]. The results showed that there was no evident difference between broad-spectrum penicillin with or without beta lactamase inhibitors and 1st and 2nd generation cephalosporins for postoperative wound infection. Concerning the comparison of broad-spectrum penicillin plus beta lactamase versus 1st and 2nd generation cephalosporins, there was only one study[17] comparing amoxycillin/clavulanic acid(AMX/CL) with cefazolin and there was no significant difference between the two groups in preventing wound infection. Although AMX/CL had activity against potential pathogens, it was not superior to cefazolin in preventing infection. Regarding the cost, the use of AMX/CL is more expensive. Besides, RCOG guidelines had indicated that AMX/CL is not recommended due to the increased risk of necrotizing enterocolitis[31]. Because of a substantial heterogeneity in broad-spectrum penicillins group, the three articles, we according to the subclasses of cephalosporins, region, dosage regimen subgroup analyses, the results showed: (1) The comparison of P2 versus C1 remained heterogeneous, the comparison of P2 versus C2 is too few to analyze, to a certain extent, the subclasses of cephalosporins may not be a source of heterogeneity; (2) The region was not a source of heterogeneity; (3) Mivumb's and Fang's studies[18,20] were single-dose regimen, while only one study [19] was multiple-day dose regimen. Depending on the results, the dosage regimen may be a source of heterogeneity. In support of our hypothesis, the study of zhang was removed, leaving two studies with homogeneity. We conducted a meta-analysis on the remaining two articles(Fig. 11). Although there was no statistical difference, cephalosporins were slightly superior to broad-spectrum penicillins in preventing wound infection(RR 3.00, 95% CI 0.84–10.73, $I^2 = 3.0\%$, p = 0.09). At present, it is generally accepted that single-dose regimen was better utilized for prevention.
The results showed that there were no differences between the broad-spectrum penicillins with or without beta-lactamase inhibitors and 1st and 2nd generation cephalosporins for preventing post-caesarean urinary tract infection and febrile morbidity. Concerning postpartum urinary tract infection, in addition to the prophylactic antibiotics, post-cesarean bacteriuria may be further reduced by avoiding routine catheterization.

In terms of safety, two articles\[12,13\] reported the events of maternal rashes, there was no evident difference between groups regarding antibiotic-related rashes. 3 patients were found in ampicillin/sulbactam group and 1 in the cefotetan group. Patients developed a rash that resolved following two doses of diphenhydramine hydrochloride. Overall, the safety of drugs in each group was good.

Antibiotics exposure may adversely effect the newborn's developing immune system and microbiome. As the links between gut microbiota composition and behaviour become more established through both clinical and preclinical studies, research has begun to focus on the effects of microbiota disruption during critical windows of development, including the perinatal period\[32\]. Rory's team\[33\] observed in perioperative animal models that early life exposure to maternal antibiotics(a single, low-dose penicillins) led to persistent alterations in anxiety, sociability and cognitive behaviours. They suggested that change in the gut microbiome is a potential mechanism for behavioural and physiological changes. While extrapolating data obtained in rodent models to humans is not simple, these data support the view that there are potential long-term detrimental consequences of maternal antibiotic use in the perinatal period. Currently, monitoring of adverse events in offspring after maternal antibiotic use is usually limited to the duration of treatment and the short period thereafter, without long-term monitoring. Therefore, unfortunately, no neonatal adverse effects were reported in the included studies. It is enlightening to us that the adverse effects on neonates need to be assessed by collecting long-term data. So far, there is relatively little research in this aspect, and we can conduct more in-depth exploration in this direction in the future, which are important evidence for evaluating antibiotic safety.

The limitations of this analysis

(1) part of the studies lacked information on study design which may increase the risk of deviation; (2) some outcome indicators have been reported in only one literature that was not available for meta-analysis; (3) earlier trials in this study administered antibiotics at or immediately after the umbilical cord clamping, with timing difference from the currently supported administration prior to skin incisions, so the results may influence the recommendation for prophylaxis at present.

Conclusions

This meta-analysis includes relatively new, comprehensive studies that provide a more appropriate recommendation for the prophylaxis of antibiotics in cesarean section. Broad spectrum penicillins with or without beta-lactamase inhibitors and 1st and 2nd generation cephalosporins may have similar efficacy in prevention of post-caesarean infections. Broad spectrum penicillins such as ampicillin and 1st or 2nd generation cephalosporins are good choices of prophylactic antibiotics for cesarean section, they are equally effective, safe and inexpensive. But, the use of the wider spectrum antimicrobial such as ampicillin/sulbactam was not superior to the more narrow spectrum 1st and 2nd generation cephalosporin
and may promote antimicrobial resistance. There were a few adverse reactions and no severe infectious complications reported among the 1,998 women included in the analysis. Adverse effects on newborns need to be assessed by collecting long-term data.

**Declarations**

**Authors’ contributions** Qianqian Song: project development, data collection, data analysis, manuscript writing. Jingjing Yan: data collection, data management. Na Bu: data collection, data analysis. Weidong Fei: project development, critical revision of the manuscript.

**Funding** *This work was supported by* the Natural Science Foundation of Zhejiang Province (*Grant numbers*[LQ20H300002])

**Conflict of interest** The authors declare that they have no conflicts of interest.

**Ethical approval** Not applicable.

**Consent to participate** Not applicable.

**Consent for publication** Not applicable.

**References**


Figures
Figure 1

Study flow diagram
Figure 2

Risk of bias summary
Figure 3
Risk of bias graph

Figure 4
Forest plot of the incidence of endometritis comparing P2+ with C1&C2.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>penicillins plus betalactamase inhibitors</th>
<th>cephalosporins C1 and C2</th>
<th>Risk Ratio</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
</tr>
<tr>
<td>Bracare 1997</td>
<td>1</td>
<td>87</td>
<td>1</td>
</tr>
<tr>
<td>Randowd 2003</td>
<td>0</td>
<td>33</td>
<td>1</td>
</tr>
<tr>
<td>Japan 2010</td>
<td>3</td>
<td>55</td>
<td>2</td>
</tr>
<tr>
<td>Zeppes 2010</td>
<td>6</td>
<td>81</td>
<td>4</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>10</td>
<td>266</td>
<td>6</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 0.86; df = 3 (P = 0.97); I² = 0%
Test for overall effect: Z = 0.96 (P = 0.33)

Figure 5
Forest plot of the incidence of wound infection comparing P2+ with C1&C2.

Figure 6
Forest plot of the incidence of urinary tract infection comparing P2+ with C1&C2.

Figure 7
Forest plot of the incidence of maternal rashes comparing P2+ with C1&C2.

Figure 8
Forest plot of the incidence of endometritis comparing P2 with C1&C2.
Forest plot of the incidence of wound infection comparing P2 with C1&C2.

Figure 10

Subgroup analysis the incidence of wound infection comparing P2 with C1&C2 according to subclasses of cephalosporins, region, dosage regimen.

Figure 11

Forest plot was obtained after the removal of one article from heterogeneous sources.

Figure 12

Forest plot of the incidence of febrile morbidity comparing P2 with C1&C2.