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RESEARCH ARTICLE

Overuse of prophylactic antibiotics for elective caesarean delivery in Medani Hospital, Sudan [version 1; peer review: 2 approved with reservations]

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Abstract

Background: Antibiotics for prophylaxis are widely used to reduce the risk of post-caesarean delivery infection. The dosage regimens are often inappropriate and may result in the appearance of drug-resistant organisms, which will increase the cost.

Objectives: A cross-sectional study was conducted to investigate the prescribing patterns of prophylactic antibiotics for elective caesarean delivery (CD) at Medani Hospital, Sudan.

Method: The medical records of women who underwent elective CD from April 2015 to June 2015 were reviewed retrospectively.

Results: The main reasons for CD among these women (n=202) were repeat CD, breech and antepartum haemorrhage. The mean ($\pm$ SD) age of the women was 28.7 ($\pm$ 6.2) years. Ceftriaxone was the most commonly prescribed antibiotic, prescribed for 63.9% of women. It was used alone in 12.4% of cases, and in combination with gentamicin and metronidazole in 49.5% of cases. Cefuroxime was used in combination with gentamicin and metronidazole in 26.7% of women, and in combination with metronidazole only in 9.4% of women, making the overall percentage 36.1%. Antibiotics were administered for 5 days in 32.7% of cases. 91.1% of women received antibiotic prophylaxis after clamping of the cord. All women received oral antibiotic prophylaxis on discharge for five to seven days. Oral cefuroxime in combination with metronidazole was the most preferred regime (77.2 %).

Conclusions: The current study shows overuse of antibiotics for elective CD. Injectable ceftriaxone in combination with gentamicin and metronidazole after cord clamping was the most commonly prescribed regime.

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2. **Musa Sekikubo**, Makerere University,
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Any reports and responses or comments on the article can be found at the end of the article.

Keywords

antibiotics, caesarean delivery, ceftizoxime, metronidazole

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Author roles: **E. Abbas T:** Conceptualization, Formal Analysis, Investigation; **Adam I:** Conceptualization, Validation, Writing – Original Draft Preparation; **M. Elhassan E:** Supervision, Writing – Original Draft Preparation; **M. Tag Eldin IE:** Investigation, Supervision, Writing – Original Draft Preparation; **Abdel Rahman M:** Data Curation, Supervision, Writing – Original Draft Preparation

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Introduction

Cesarean delivery (CD) is a procedure mainly performed to save the lives of mother and child to ensure a healthy outcome when normal vaginal delivery is not possible. It is the most common major surgical procedure performed worldwide (Blanchette, 2011; DeFrances & Hall, 2007). With increasing CD rates, postpartum maternal infections are likely to become an increasing health and economic burden and their prevention remains a public health priority (Martin *et al.*, 2010). Postpartum endometritis and abdominal wound infections are the most common infectious complications following childbirth, and their incidence has increased due to CD becoming a routine procedure (Chaim *et al.*, 2000).

The Cochrane Database of Systematic Reviews has reported that antibiotic prophylaxis has reduced the risk of infectious morbidity of CD by 50% to 70% (Smaill & Grivell, 2014; Tita *et al.*, 2009). The hospitals that used antibiotic prophylaxis for elective CD demonstrated high compliance and decreased rates of postpartum infectious complications (Skjeldstad *et al.*, 2015). The desired antibiotic used for prophylaxis should have maximum efficacy against the organism at the surgical site, have a long duration of action and be delivered at an acceptable dose. (Burke, 2001).

Recent reports have shown that a single dose of antibiotic used for CD is equally as adequate as multiple doses or multiple antibiotics, reducing the cost without increasing the infection rate (Gidiri & Ziruma, 2014; Ijarotimi *et al.*, 2013; Westen *et al.*, 2015a). Prolonged use of prophylactic antibiotics can lead to emergence of resistant bacterial strains (Harbarth *et al.*, 2000).

Administration of antibiotic prophylaxis prior to CD is as effective as when given after cord clamping in reducing the risk of infectious morbidity (Costantine *et al.*, 2008; Lamont & Joergensen, 2014). Various epidemiological studies have been conducted in different countries to assess the use of prophylactic antibiotics in a clinical setting (Gouvêa *et al.*, 2015; Huskins *et al.*, 2001). In Sudan, almost

two fifth of babies are being delivered by caesarean (Abbaker *et al.*, 2013). In spite of this high rate, there are few published studies on the effects of antibiotic prophylaxis for CD in Sudan (Ahmed *et al.*, 2004; Elbur *et al.*, 2014; Osman *et al.*, 2013). Therefore, we investigated the prescription patterns of prophylactic antibiotics for elective CD at Medani Hospital, Sudan.

Methods

A cross-sectional study was conducted at Medani Hospital, Sudan by reviewing medical records of women who underwent elective CD at Medani Maternity Hospital, Sudan from April to June 2015. Medical records were taken from the Hospital Medical Archive system. The hospital owns the patient records that were accessed. The data were managed anonymously. Thus, the files were reviewed and patient consent was not being necessary. The Review Board of Medani Maternity Hospital Medical, Sudan approved the use of the data (# 2015/26). Data collected includes age, parity, indication for CD, type of anaesthesia given (general or spinal), time at which prophylactic antibiotics were administered (during induction of anaesthesia or after cord clamping), type and strength of injectable antibiotic prescribed, duration of treatment, and the regimen of oral antibiotic given after discharge from the hospital.

Statistical analysis

The sample size of 202 women was estimated according to the equation: $n = (Z_{1-\alpha})^2 (P(1-P)/D^2)$.

SPSS for Windows version 20.0 was used for data analysis. Continuous and categorical data were expressed as mean ($\pm$ SD) and as proportions, respectively.

Results

202 medical records were reviewed. The mean ($\pm$ SD) of the age was 28.7 (6.2) years. The main indications for the operation were repeat CD, previous miscarriage and intrauterine fetal death (Figure 1).

Figure 1. Indications for elective caesarean delivery at the Medani Hospital, Sudan.

The mean ($\pm$ SD) duration of antibiotic treatment was 6.4 ($\pm$ 1.3) days. Ceftizoxime was the most commonly prescribed antibiotic, at an overall rate of 63.9%. It was used alone in 12.4% of cases, and in combination with gentamicin and metronidazole infusion in 49.5% of cases. In 2% of the women, ceftizoxime was administered in combination with metronidazole alone. The second most common regime involved cefuroxime. It was used in combination with gentamicin and metronidazole infusion in 26.7% of women, and it was administered with metronidazole only in 9.4% of women.

The majority (91.1%) of women received antibiotic prophylaxis after clamping of the cord. All patients received oral antibiotic prophylaxis after discharge, for five to seven days. Oral cefuroxime (zinoxamore) in combination with metronidazole was the most prescribed regimen (77.2%).

Dataset 1. Raw data collected as the basis for this study

<http://dx.doi.org/10.5255/f1000research.11919.d168395>

Discussion

Antibiotic prophylaxis for caesarean delivery

The main finding of the current study was that multiple regimens for antibiotic prophylaxis were being administered to women undergoing elective CD at the Medani Maternal Hospital. The use of antibiotic prophylaxis for CD has been shown to be effective in reducing post-operative morbidity, cost and duration of hospitalization (Clifford & Daley, 2012; Smaill & Grivell, 2014; Tita *et al.*, 2009).

Duration of antibiotic prophylaxis for caesarean delivery

The duration of prophylactic treatment administered to the women at Medani Maternal Hospital was extended to an average of 6.4 days. This is inconsistent with international guidelines, where a short duration of prophylaxis (usually < 24 hours) is recommended, and it gives the benefit of minimal toxicity and decreases the risk of antibiotic resistance (Dellinger *et al.*, 1994; Giuliani *et al.*, 1999). A number of studies have concluded that a single dose regime was equally as effective as multiple dose regimes. (Bhattachan *et al.*, 2013; Westen *et al.*, 2015b; Ziogos *et al.*, 2010)

International and global clinical guidelines have been prepared by a number of advisory committees on the use of antibiotic prophylaxis for women undergoing CDs. Evidence-based recommendations for the prevention of surgical site infections (Berríos-Torres *et al.*, 2017; Review, 2017) state that antibiotic prophylaxis should be administered before skin incision, and no additional doses should have to be administered after the surgical incision is closed (Bhattachan *et al.*, 2013; Ziogos *et al.*, 2010). The guidelines from the American Society of Health-System Pharmacists (ASHP), recommend the use of a single dose of cefazolin administered before surgical incision (Bratzler *et al.*, 2013). Clinical Practice Guidelines approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada recommends the use of a single dose of a first-generation cephalosporin, 15 to 60 minutes prior to skin

incision, with no additional doses (van Schalkwyk *et al.*, 2010). A national clinical guideline developed by the Scottish Intercollegiate Guidelines Network for antibiotic prophylaxis in surgery recommends the use of a single standard dose of narrow-spectrum, more affordable antibiotics for prophylaxis (Scottish Intercollegiate Guidelines Network, 2008).

Although many national and international guidelines recommend the use of a single dose of antibiotic for prophylaxis, in our study the average duration of prophylaxis is extended to five-seven days, which is of concern. Antibiotic prophylaxis in surgery is used for prevention of surgical site infections, with optimal use involving the use of the antibiotic agent at a dosage that ensures adequate serum and tissue concentrations during the period of potential contamination (Burke, 2001). The antibiotic should be administered for the shortest feasible period to minimize the risk of adverse effects, development of resistance, and costs. Therefore, there is no need for an extended duration for antibiotic use, as observed in this study.

Gurusamy and his colleagues have demonstrated that multiple prophylactic antibiotics or an increased duration of antibiotic prophylaxis is of no advantage to surgical patients with respect of reduction of MRSA infection (Gurusamy *et al.*, 2013). The administration of single dose antibiotic prophylaxis also reduces the load on the staff and decreased the costs, which is a good for low-resource settings, and should be adopted if the cost has to be reduced (Gidiri & Ziruma, 2014; Ijarotimi *et al.*, 2013; Westen *et al.*, 2015a).

The prolonged use of prophylactic antibiotics can lead to emergence of resistant bacterial strains (Harbarth *et al.*, 2000). The indiscriminate use of antibiotic prophylaxis coupled with the great capacity of adaptation of microorganisms, enables the emergence of resistant strains, which requires, synthesis of increasingly expensive drugs, resulting in significant increases in healthcare costs.

Injectable ceftizoxime in combination with gentamicin and metronidazole after cord clamping was the most commonly prescribed regime in our study. The second-generation cephalosporin cefuroxime in combination with metronidazole was used as the second most common regime. In a similar study, Elbur and colleagues found great variation in prescribing patterns between different obstetrics units in Khartoum (Elbur *et al.*, 2014).

The use of third generation cephalosporins, imidazole derivatives and second generation cephalosporins resemble the patterns seen in Asian countries where broad spectrum cephalosporin use is predominant (Al-Momany *et al.*, 2009; Mahdaviyazad *et al.*, 2011). Inappropriate use of both prophylactic and therapeutic antibiotics in surgical procedures was observed in Malaysia (Lim *et al.*, 2015). John J *et al.*, also demonstrated inappropriate use of antibiotics in patients undergoing gynaecologic surgery in Texas (Joyce *et al.*, 2017). In spite of this, many developed countries prefer the use of first generation cephalosporins or a combination of penicillin and betalactamase-inhibitors (Durando *et al.*, 2012; Hosoglu *et al.*, 2009). The inappropriate use of antibiotics may result in

the development of drug-resistant organisms, which is concerning. (Dancer, 2004). The overuse of third-generation cephalosporin leads to the development of new strains of extended spectrum beta-lactamases (ESBLs), MRSA, vancomycin-resistant enterococci (VRE), and *Clostridium difficile* (Dancer, 2001).

Time of administration of antibiotic prophylaxis for caesarean delivery

Our study revealed that the majority (91.1%) of women received antibiotic prophylaxis after clamping of the cord. However, less surgical wound infections have been observed when antibiotics were administered prior to skin incision, and there was no increase in the adverse effects on the neonates. (Dlamini *et al.*, 2015; Lamont & Joergensen, 2014; Tita *et al.*, 2009).

Conclusions

The current study shows an overuse of antibiotics for elective CD. Injectable ceftizoxime in combination with gentamicin and

metronidazole after cord clamping was the most commonly prescribed regime at Medani Hospital, Sudan.

Data availability

Dataset 1: Raw data collected as the basis for this study. DOI, 10.5256/f1000research.11919.d168395 (Adam *et al.*, 2017).

Ethical approval

The study was approved by the Review Board of the Medani Maternity Hospital Medical, Sudan (# 2015/26).

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no grants were involved in supporting this work.

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Musa Sekikubo

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It is difficult to evaluate antibiotic overuse without reference to locally available guidelines on prophylaxis.

There are mixed thoughts on the timing of prophylactic antibiotics¹ - 30 minutes prior to incision vs after clamping the cord - what do the local guidelines recommend? It is not clear what was done in patients with preterm rupture of membranes.

The design seemed more of a retrospective records review than a cross sectional study.

The results don't spur future practice as they can not be pegged against current guidelines.

Recommendations:

- The study could benefit from additional information on local guidelines on antibiotic prophylaxis during Caesarean section to enable the reader to compare adherence to guidelines.
- I have significant reservations about the study despite its importance in the era of increasing antibiotic resistance.

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Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Maternal infectious diseases

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 15 November 2017

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Hansa Dhar

Clinic of Obstetrics and Gynecology, Nizwa Hospital, Nizwa, Oman

The above research is a very relevant topic of concern as the authors have truly highlighted the advantages of prophylactic antibiotics in caesarean sections in the recent age. Prophylactic antibiotics have reduced the complications of post-operative wound infection, maternal infections, endometritis and pyrexia in caesarean delivery.

In this study various drugs as prophylaxis with different durations have been used.

But there is no comparative study of prophylactic drug regimes and drug durations for which these drugs were used in the hospital.

The correct prophylactic regime accepted world wide is a single second generation cephalosporin (cefazoline) used within 30 minutes to one hour prior to surgery which is helpful in avoiding postoperative infections.

The regimes used in the above study appear to be therapeutic rather than prophylactic.

A comparative study highlighting the advantages versus disadvantages of the overuse of the various multiple drug regimes in post operative follow up of these cases would improve the study. Patients who had postoperative complications if any has not been noted in the results, thereby

making it an incomplete study.

Recommendations =

- 1.The study needs to be elaborated further.
- 2.Comparative study of all the drug regimes need to be done.
3. Complications observed in study group should be noted.
4. Graphic representation in the form of a table should be added after comparison of all regimes.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

No

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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