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CLINICAL ARTICLE

Prophylactic ampicillin versus cefazolin for the prevention of post-cesarean infectious morbidity in Rwanda

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ABSTRACT

Objective: To evaluate the efficacy of ampicillin versus cefazolin as prophylactic antibiotics prior to cesarean delivery in Rwanda. *Methods:* In a prospective, randomized, open-label, single-site study conducted between March and May 2012, the effects of prophylactic ampicillin versus cefazolin were compared among women undergoing cesarean delivery at the Centre Hospitalier Universitaire de Kigali, Rwanda. Postoperatively, participants were evaluated daily for infectious morbidity while in the hospital. Follow-up was done by phone and by appointment at the hospital within 2 weeks of delivery. *Results:* During the study period, there were 578 total deliveries and 234 cesarean deliveries (40.4%). Overall, 132 women were enrolled in the study and randomized to receive either ampicillin (n = 66) or cefazolin (n = 66). No women were lost to follow-up. The overall infection rate was 15.9% (21/132). The infection rate in the ampicillin group and the cefazolin group was 25.8% (17/66) and 6.1% (4/66), respectively. *Conclusion:* Implementing a universal protocol in Rwanda of prophylactic cefazolin prior to cesarean delivery might reduce postoperative febrile morbidity, use of postoperative antibiotics, and number of postoperative days in hospital.

1. Introduction

Cesarean delivery is the most common operation in obstetric practice. The incidence of cesarean delivery is rising worldwide: in 2010, the reported incidence ranged from 0.4% in Chad to 45.9% in Brazil [1]. In the USA, the rate increased from 5% in 1970 to nearly 32.8% in 2010 [2], whereas that in Rwanda was estimated at 12.5% in 2010 [3]. The risk of postoperative infectious morbidity after cesarean delivery without antibiotic prophylaxis ranges from 4.6% for women undergoing elective cesarean to 20%–85% for women undergoing cesarean delivery after labor or rupture of membranes [4]. Overall, women who have a cesarean delivery have a risk of infection that is 5–20-fold greater than that of women having a vaginal delivery [5].

Infectious morbidity, such as endometritis and wound infection, constitutes most of the complications of cesarean delivery, and its incidence varies depending on whether or not the surgery is scheduled. Wound infection typically presents on postoperative days 3–5, and is usually preceded by induration and erythema around the skin incision. In the USA, depending on the population studied, 2.8%–26.6% of women undergoing cesarean delivery are reported to develop a postoperative wound infection [6]. A report from a district hospital in Kenya revealed a rate of wound infection of 19% in 2005 [7], whereas a report from a teaching hospital in Nigeria demonstrated a rate of 9.1% in 2012 [8].

The occurrence of post-cesarean infection is associated with a longer duration of hospitalization and an increase in healthcare costs. Many techniques to decrease wound infection have been investigated including perioperative intravenous and/or irrigation antibiotic prophylaxis, skin preparation techniques, subcutaneous suture closure, subcutaneous drainage, and skin incision techniques. Recent reviews have confirmed that, compared with placebo, prophylactic antibiotics for women undergoing cesarean delivery are effective in decreasing the incidence of febrile morbidity related to endometritis, wound infection, and urinary tract infection. On the basis of numerous studies, the use of prophylactic antibiotics with cesarean delivery is widely validated and accepted [5,9,10]. When used prophylactically, a single broad-spectrum antibiotic seems to be as effective as a combination of 2 or more antibiotics [11].

As in much of the world, cesarean delivery rates are increasing in Rwanda for various reasons. The Centre Hospitalier Universitaire de Kigali/University Teaching Hospital of Kigali (CHUK), which is located in Kigali, the capital of Rwanda, is 1 of 3 tertiary care referral hospitals in the Rwandan healthcare system and, compared with district hospitals, receives a disproportionate number of patients needing cesarean deliveries. Of its approximately 170 obstetric deliveries per month, 45.8% are spontaneous vaginal deliveries and 54.2% are cesarean deliveries. With the rising cesarean rate, the incidence of postoperative

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infectious complications is also likely to increase. To date, there have been no studies conducted in Rwanda on the incidence of postoperative infectious morbidity after cesarean delivery.

Cefazolin, a first-generation cephalosporin, has been shown to have good activity against many of the pathogens associated with post-cesarean infectious morbidity. In addition to its antimicrobial profile, this parenteral drug also has advantageous pharmacokinetics for this indication [11,12]. For these reasons, in addition to cost, cefazolin has been recommended as a single-agent antimicrobial prophylaxis for cesarean delivery.

In Rwanda, the use of prophylactic and postoperative antibiotics is markedly variable with some practitioners prescribing routine postoperative antibiotics for 3, 5, or even up to 7 days after a cesarean delivery. There are few standardized protocols for hospital use. Although cefazolin has been demonstrated to be a good prophylactic agent for cesarean delivery in other countries [13], its standardized use in Rwanda has not been studied. Ampicillin is more typically the antimicrobial of choice, but its effectiveness has been questioned and it is essential to investigate whether or not other antibiotics are needed. The aim of the present study was to evaluate the efficacy of single-dose ampicillin (the most commonly used agent) versus single-dose cefazolin as prophylactic antibiotics prior to cesarean delivery in Rwanda.

2. Materials and methods

The present prospective, randomized, open-label, single-site study recruited pregnant women undergoing cesarean delivery at CHUK, Kigali, Rwanda, between March 1 and May 31, 2012. The study was approved by the research and ethics committee of the Faculty of Medicine at CHUK. All women were required to sign an informed consent form that explained the risks and benefits of this research. They were informed about their right to refuse participation in the study without any change in the care that they would receive. All information obtained from participants was treated confidentially and used only for research purposes.

The sample size was based on an estimated incidence of post-cesarean wound infection of 14% in accordance with the current standard of care in Rwanda. This estimate was derived from an average of recent Nigerian and Kenyan data [7,8]. The study aimed to demonstrate a 50% reduction in the incidence of wound infection from 14% to 7% with an α error of 5% and β error of 50%. This gave a sample size of 66 women in each arm (132 women in total).

The inclusion criterion was cesarean delivery for any indication at a gestation of 37 weeks 0 days or more. The exclusion criteria were a preoperative clinical diagnosis of chorioamnionitis, a fever of 38° or higher at any point during admission, prior antibiotic use within 2 weeks, known HIV-positive status, known allergy to penicillin or cephalosporin, and insulin-dependent diabetes.

After providing informed consent, the women were preoperatively randomized to 1 of 2 study groups via numerically ordered cards in sealed envelopes. The cards inside the envelopes were randomized by the principle investigator using a random integer generator [14]. The allocated envelopes were opened by clinicians only after the decision for cesarean delivery was made. Women in the ampicillin group (usual care group) received a single dose of 2 g of ampicillin administered intravenously no more than 60 minutes prior to skin incision. Those in the cefazolin group received a single dose of 1 g of cefazolin administered intravenously no more than 60 minutes prior to skin incision. Postoperative antibiotics were administered only if there was a diagnosis of infection, and were not given routinely.

Postoperatively, women were seen by one of the study investigators; however, all management decisions including timing of discharge were made by the patient's attending physician. Patient temperatures were recorded daily. All surgical dressings were evaluated between 48 and 72 hours after surgery. Where indicated, women with an infection had blood, urine, and/or wound samples taken for culture. Those with benign examinations were routinely discharged after 3 days and

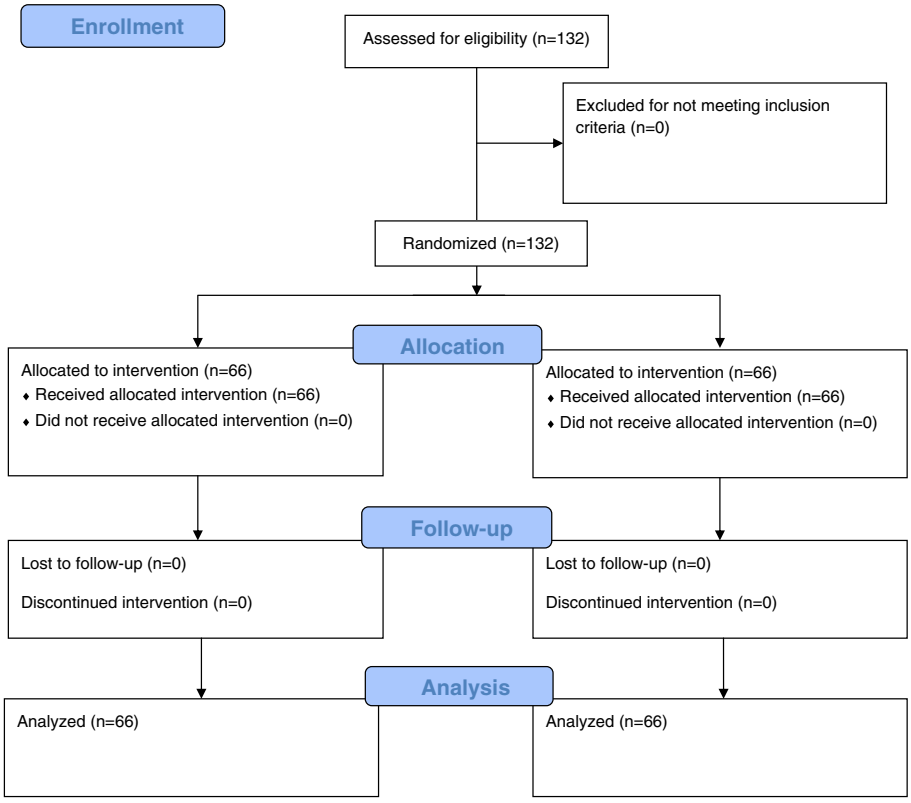

Fig. 1. Flow of participants through the study.