e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(9); 238-243

Original Research Article

Effectiveness of Prophylactic Antibiotic Administration using Cefoxitin at the Time of Elective Caesarean Section: A Randomized Controlled Clinical Assessment

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Received: 14-04-2023 / Revised 29-05-2023 / Accepted 15-07-2023

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Conflict of interest: Nil

Abstract:

Aim: The aim of the present study was to determine whether prophylactic antibiotic administration using cefoxitin at the time of elective caesarean section significantly reduces infectious morbidity.

Methods: The present study was conducted in the Department of Obstetrics and Gynecology for two years .Two hundred women undergoing elective caesarean section had cefoxitin or placebo administration after umbilical cord clamping. Postpartum complications including febrile morbidity, wound infection, endometritis, urinary tract infection, pneumonia and transient postpartum fever were recorded, as were the duration of hospital stay and the need for therapeutic antibiotics.

Results: The two groups were similar with respect to age, parity, gestational age, weight and pre- operative haemoglobin values. Ten women (10%) in the placebo group and 12 women (12%) in the cefoxitin group were antibody positive for the human immunodeficiency virus (HIV). Women who had two or more previous caesarean sections constituted just over half the women in each group and the second most common indication of one previous caesarean section accounted for about a third of the cases. The operator status, type of anaesthetic, type of skin incision, length of surgery, the presence of adhesions, and the type of skin closure were not significantly different between the groups. Over 90% of women in both groups were operated on by a registrar, had spinal anaesthesia and their duration of surgery was less than an hour. There were fewer women in the placebo group who had skin wound drains compared with the cefoxitin group.

Conclusion: Antibiotic prophylaxis with cefoxitin in elective caesarean section did not reduce post-operative infectious morbidity in this double-blind randomised placebo controlled trial. We suggest that prophylactic antibiotics in elective caesarean section be restricted to women who have a high body mass index and where the baseline infectious morbidity is > 15%.

Keywords: Prophylactic Antibiotic, Cefoxitin, Elective Caesarean Section.

Introduction

Infectious maternal and perinatal morbidities are 5 to 20 times more in caesarean section when compared to vaginal births. [1] Genital tract is most important source of infections particularly when membrane is ruptured and also even if membranes are intact, polymicrobial invasion of intrauterine cavity occurs especially with preterm labour. [2] The purpose of prophylactic antibiotic in surgeries is not for sterilization of tissue but for reducing colonization of microorganisms introduced during operation to a level to overcome by patient's immunity. [3] Broad spectrum antibiotic like cephalosporins are most commonly administered for SSI prophylaxis. [4] The dosage should be adequate to exceed minimum inhibitory concentration (MIC) for the organism likely to be encountered during the operation. Prophylactic antibiotic during caesarean delivery has usually been given after umbilical cord clamping for apprehension of fetal exposure through placenta if administered earlier.

Postoperative infectious morbidity prolongs hospitalization and increases the overall burden and cost of surgery both on the individual and community levels. Estimates of prolonged hospitalization vary from 5 to 20 days per infection. [5-7] Maternal postoperative infectious morbidity is much more likely to follow Cesarean

delivery compared to normal labor. [8] Hence, the importance of prophylactic antibiotic utilization in order to protect against or minimize the risk of such morbidity. Although a lot of information about the role of prophylactic antibiotics in reducing infectious morbidity after Cesarean is available in the literature, they are all derived from rich/adequate health resource settings in the industrialized countries. Such data cannot be generalized and applied to patients in low resource settings. [9]

In low settings and despite the possible availability of skilled obstetricians and nurses all around the clock, other factors may intervene to affect the quality of health service provided and their outcome. Factors such as non-availability of some drugs or suture materials, broken or overused instruments, interruption of electricity and refrigeration, occasional cut of water supply may have major impacts on the outcome of a successful surgery. In addition, the patient in a low resource setting is usually poor, illiterate or has minimal education. Such patient lacks the principles of self-hygiene and personal cleanliness. She can be improperly nourished and anemic as well, a factor that might lead to defective healing or possible infection. Another important factor is smoking which reduces tissue oxygenation[9] and may therefore predispose to surgical wound infection. Although prohibited in hospitals in rich settings, smoking remains a major problem in hospitals at low resource settings.

The aim of the present study was to determine whether prophylactic antibiotic administration using cefoxitin at the time of elective caesarean section significantly reduces infectious morbidity.

Materials and Methods

The present study was conducted in the Department of Obstetrics and Gynecology, Patna Medical College and Hospital, Patna, Bihar, India for two years .Two hundred women undergoing elective caesarean section had cefoxitin or placebo administration after umbilical cord clamping. Postpartum complications including febrile morbidity, wound infection, endometritis, urinary tract infection, pneumonia and transient postpartum fever were recorded, as were the duration of hospital stay and the need for therapeutic antibiotics.

The exclusion criteria were mothers who had received antibiotics in the preceding two weeks, those with a history of allergy to penicillin or cephalosporin, and those with rupture of membranes. The study was designed as a randomised double-blind, placebo- controlled trial.

The required sample size was based on an assumption of a risk ratio of at least 0.3 for the antibiotic group using a 12% baseline febrile morbidity rate for elective caesarean section. The study would therefore require 236 women per group to show statistical significance at the 5% level with 90% power. Randomisation of 480 women was carried out by a computer-based allocation of each study number to either cefoxitin or placebo. Allocation to either placebo or cefoxitin were placed in consecutively numbered sealed envelopes and only opened by the pharmacist on the day of surgery.

The hospital pharmacist prepared a solution of placebo or cefoxitin according to the random schedule and the coded solutions were given to the anaesthetist in theatre. Neither the medical, nursing staff or the patient knew which agent was given. The pharmacist held the randomisation code in the eventuality of an anaphylactic reaction. The pharmacist prepared the placebo solution with 25mg mannitol and 25mg riboflavin to provide a pale yellow colour such that it was indistinguishable from the solution of 2g of cefoxitin. The prepared solutions were handed over to the anaesthetist to administer after umbilical cord clamping at caesarean section. All caesarean sections were performed by a standard technique and all post-operative care followed standard clinical practice.

The following postpartum complications were recorded: 1. febrile morbidity defined as oral temperature of > 38°C on two occasions six hours apart excluding the first 24 hours following surgery; 2. wound infection (the presence of wound cellulitis, erythema, serous, serosanguinous and/or purulent discharge, with or without fever, and with or without positive cultures from the wound site); 3. endometritis (fever, uterine tenderness and malodorous lochia); 4. urinary tract infection (fever and positive urine culture); 5. pneumonia (fever and abnormal clinical and/or chest radiological findings); 6. transient postpartum fever (febrile morbidity not associated with an infective focus).

The duration of hospital stay, the need for therapeutic antibiotics and all neonatal data were recorded. In women with pyrexia, blood cultures were taken. Wound morbid- ity was managed by local wound toilet with hydrogen peroxide and saline irrigation. In cases of purulent wound discharge, microbiological specimens were taken and antibiotic therapy instituted in cases with associated febrile morbidity or on the outcome of culture and sensitivity results. On discharge from hospital, women were informed to report any fever, wound dehiscence or foul smelling lochia immediately, and all women were seen at the six week postnatal visit for evidence of wound dehiscence.

Statistics: The data were analysed using Stata Release 5 (Stata Corporation. 1997; Stata Stateside Software College Station, Texas, USA). For all categorical variables Fisher's Exact test or y^2 was used. For continuous variables Student t test was performed. The results are reported as relative risk (RR) or risk differences with 95% confidence intervals (CI).

Results

Table 1: Patient demographics

Parameters	Placebo n=100	Cefoxitin n=100
Age (years) Mean (SD)	31.19 (5.4)	30.2 (5.8)
Gestational age (wks) Mean (SD)	38.4 (1.6)	38.6 (1.4)
Body weight (kg) Mean (SD)	82.8 (16.4)	83.5 (16.6)
Pre-operative Hb (g/dl) Mean (SD)	11.9 (1.2)	10.9 (1.4)
HIV positive	10 (10)	12 (12)

The two groups were similar with respect to age, parity, gestational age, weight and pre- operative haemoglobin values. Ten women (10%) in the placebo group and 12 women (12%) in the cefoxitin group were antibody positive for the human immunodeficiency virus (HIV).

Table 2: Indications for caesarean section (CS)

Indications	Placebo n=100 (%)	Cefoxitin n=100 (%)
1 previous CS	30 (30)	32 (32)
≥2 or more previous CS	55 (55)	54 (54)
IUGR	2 (2)	0
Hypertension	3 (3)	8 (8)
Diabetes	1 (1)	1 (1)
Breech	1 (1)	1 (1)
Big baby (> 4 kg)	1 (1)	2 (2)
Others	6 (6)	2 (2)

Women who had two or more previous caesarean sections constituted just over half the women in each group and the second most common indication of one previous caesarean section accounted for about a third of the cases.

Table 3: Operation/surgical characteristics

Operation/surgical characteristics	Placebo n=100 (%)	Cefoxitin n=100 (%)
Surgeon		
Registrar	98 (98)	97 (97)
Consultant	2 (2)	3 (3)
Anaesthetic		
General	3 (3)	94 (94)
Spinal	95(95)	1 (1)
Epidural	2 (2)	5 (5)
Skin incision		
Pfannensteil	55 (55)	64 (64)
Midline sub umbilical	45 (45)	36 (36)
Suture	54 (54)	46 (46)
Subcutaneous	44 (44)	52 (52)
Other	2 (2)	2 (2)
Skin wound drain	16 (16)	22 (22)

The operator status, type of anaesthetic, type of skin incision, length of surgery, the presence of adhesions, and the type of skin closure were not significantly different between the groups. Over 90% of women in both groups were operated on by a registrar, had spinal anaesthesia and their duration of surgery was less than an hour. There were fewer women in the placebo group who had skin wound drains compared with the cefoxitin group.

Table 4: Postpartum outcome

Postpartum outcome	Placebo n=100 (%)	Cefoxitin n=100 (%)
Postpartum complication	20 (20)	18 (18)
Postpartum fever	7 (7)	8 (8)
Endometritis	2 (2)	1 (1)
UTI	1 (1)	1 (1)
Pneumonia	1 (1)	1 (1)
Wound infection		

Cellulitis/erythema	3 (3)	4 (4)
Serous/seroanguinous	7 (7)	7 (7)
Purulent exudate	3 (3)	1 (1)
Wound infection with fever	5 (5)	4 (4)
Transient postpartum fever	1 (1)	2 (2)
Non-infected poor skin apposition	3 (3)	2 (2)
Blood loss > 1000ml	4 (4)	10 (10)

There was no significant difference between the study and control group with regards post-operative maternal morbidity. The administration of a prophylactic antibiotic, cefoxitin, did not significantly decrease the rate of post-operative fever, wound infection and endometritis.

Table 5: Maternal morbidity

Maternal morbidity	Placebo n=100 (%)	Cefoxitin n=100 (%)
Days in hospital	4 (4)	2 (2)
Duration of hospitalisation > 8 days	15 (15)	10 (10)
Use of therapeutic antibiotics	7 (7)	5 (5)

There was no difference in morbidity, the women who received placebo on average stayed a day longer in hospital than those who received cefoxitin (8 vs 7 days) and this was statistically significant. However, there was no difference in the number of women staying in hospital for over one week.

Discussion

Infectious morbidity is the most common complication following caesarean section with reported rates ranging from 18% to 83% [10], while that for vaginal delivery is less than 10%. [11] The potential of antibiotic prophylaxis has been studied extensively since the first controlled trial, reported by Miller and Crichton. [12] The latest systematic review and meta-analysis on antibiotic prophylaxis for caesarean section contained in the Cochrane Library included 8365 women in 66 trials. Seven trials on elective caesarean section including 875 women. The use of prophylactic antibiotics reduced the incidence of endometritis by two-thirds to three-quarters, and therefore justified its routine use for all women undergoing caesarean section. The overall rate of febrile morbidity in the untreated control group was 23%, for wound infection 7%, and for endometritis 6.4%. Although prophylactic antibiotics reduced febrile morbidity by three quarters, the rate of wound infection was not decreased (OR 0.71, 95% CI 0.39-1.30). Twenty- seven of 388 controls developed wound infection compared with 21 of 487 women who had prophylactic antibiotics. [13] American Congress of Obstetricians and Gynecologists (ACOG)[14] and The Society of Obstetricians and Gynecologists of Canada (SOGC) [15] recommended that antibiotic prophylaxis should be administered within 60 minutes before beginning CD, based on a meta-analysis which concluded that antibiotic prophylaxis before skin incision, comparing with after cord clamping, decreased the incidence of postpartum endometritis and total infectious morbidities, without affecting neonatal outcomes. [16]

The two groups were similar with respect to age, parity, gestational age, weight and pre- operative haemoglobin values. Ten women (10%) in the placebo group and 12 women (12%) in the cefoxitin group were antibody positive for the human immunodeficiency virus (HIV). Women who had two or more previous caesarean sections constituted just over half the women in each group and the second most common indication of one previous caesarean section accounted for about a third of the cases. The operator status, type of anaesthetic, type of skin incision, length of surgery, the presence of adhesions, and the type of skin closure were not significantly different between the groups. Over 90% of women in both groups were operated on by a registrar, had spinal anaesthesia and their duration of surgery was less than an hour. There were fewer women in the placebo group who had skin wound drains compared with the cefoxitin group. Another indicator of post-operative caesarean section infection is endometritis. In most studies, as in the present study, it was diagnosed on clinical grounds of fever, uterine tenderness and abnormal lochia. In some studies it is also frequently a diagnosis of exclusion, (i.e. fever in the absence of factors indicating infection elsewhere). [17] Other investigators also performed microbiological studies on amniotic fluid and endometrial scrapings. [18] Wound infection and endometritis contributed to all cases of prolonged hospital stay of more than a week. This concurs with that reported by other authors. [19,20]

The majority of the women did not have skin wound drains, and the infection rate was similar to those that had their skin wound drained. A significantly higher number of women receiving cefoxitin had uterine tears, blood loss. 1000ml and the presence of wound drains. However, there was no difference in wound infection rate between placebo and cefoxitin. It could be argued that

antibiotic prophylaxis in this group of women could have protected against infection. The majority of wound infections did not require the use of antibiotics, but were treated by local measures of wound toilet including hydrogen peroxide and saline irrigation. There was no significant difference between the study and control group with regards post-operative maternal morbidity. The administration of a prophylactic antibiotic, cefoxitin, did not significantly decrease the rate of post-operative fever, wound infection and endometritis. There was no difference in morbidity, the women who received placebo on average stayed a day longer in hospital than those who received cefoxitin (8 vs 7 days) and this was statistically significant. However, there was no difference in the number of women staying in hospital for over one week.

Conclusion

Antibiotic prophylaxis with cefoxitin in elective caesarean section did not reduce post-operative infectious morbidity in this double-blind randomised placebo controlled trial. We suggest that prophylactic antibiotics in elective caesarean section be restricted to women who have a high body mass index and where the baseline infectious morbidity is > 15%. It should also be noted that use of prophylactic antibiotics for elective caesarean section is not a panacea and should not replace proper pre- and intra-operative preparation and meticulous surgical technique. The proper surgical handling of tissues and meticulous haemostatis is probably of greater importance than prophylactic antibiotics in reducing post-operative infectious morbidity

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