# ANTIBIOTIC PROPHYLAXIS IN ELECTIVE CAESAREAN SECTION: SINGLE DOSE COMPARED TO MULTIPLE DOSE ANTIBIOTICS: A RANDOMIZED CLINICAL TRIAL

By

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Dissertation as part fulfillment of the requirements for the degree of Master of Medicine, Obstetrics & Gynaecology, University of Nairobi.

DECLARATIONS

I declare that this dissertation ismy original work and has not been submitted in any other university for award of a degree.

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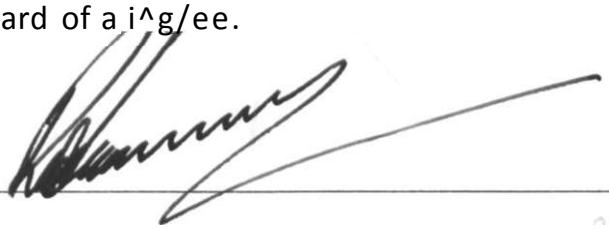
Signed  Date

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ABBREVIATIONS

| | |
|---|---|
| X-pen | Crystalline penicillin |
| K.N.H. | Kenyatta National Hospital |
| W.H.O. | World Health Organization |
| H.b. | Hemoglobin |
| C/S | Caesarean section |
| H.I.V | Human Immunodeficiency virus |
| S.U.M.I. | Sub-umbilical midline incision |
| etc | et cetera |
| e.g. | For example |
| i.e. | That is.. ' , |
| ROM | Rupture of membranes |
| ANC | Ante-natal care |
| CDC | Centre for Disease Control and Prevention |
| AIDS | Acquired Immune Deficiency Syndrome. |

DEFINITIONS

Puerperal infection: Bacterial infection in a woman after delivery.

For this study, infection of the female genital tract after elective caesarean section.

Post-partum fever: Any temperature recording of 38$^{l}$ C or more on two separate occasions at least 24 hours apart following the first 24 hours after delivery.

Endometritis: Uterine infection attended by uterine tenderness and sub-involution, fever with or without malodorous lochia.

Wound infection: Infection of the surgical wound, which may be characterized variably with erythema, tenderness, dehiscence or burst abdomen.

Severe infectious morbidity: May include septicemia, septic shock, pelvic abscesses, necrotizing fasciitis.

ABSTRACT

*Background*

The benefit of antibiotic prophylaxis in both emergency and elective caesarean section has been demonstrated repeatedly in studies, mostly in western countries. Most of these studies have not demonstrated significant differences between single and multiple dosing regimens. Single dose regimens are not generally used in Kenyatta National hospital and other public institutions.

*Objective:* To compare the incidence of any puerperal infections among women receiving a single *high* dose Crystalline penicillin plus Gentamicin intra-operatively with those receiving a three day *regular* dose Crystalline penicillin plus Gentamicin as prophylaxis during elective caesarean section at Kenyatta National Hospital.

*Study Design:* This was a Randomized, Doub|e-blinded Clinical Trial

*Study Area:* The study was conducted at Kenyatta National Hospital, Nairobi, Kenya. T

*Study population:* The study population constituted women admitted at Kenyatta National Hospital for elective Caesarean section.

*Outcome measures:* These were post-partum fever, surgical site (wound) infection and clinical endometritis. •

*Results:* 75 questionnaires were administered but only 72 were analysed (36 for each arm of the study). There were no significant differences in the socio-demographic characteristics, pre-operative obstetric characteristics and laboratory profiles. There were also no significant differences in the post-operative clinical indicators of puerperal infection, which were fever (p=l), wound infection , uterine tenderness (p=0.396)# uterine sub-involution (p=0.164) and the colour (p=0.543) and smell of lochia. Fever was the only recorded clinical indicator of infection, though this did not meet the criteria specified for post-partum febrile illness.

*Conclusion and recommendation* : A single *high-dose* of Crystalline penicillin and gentamicin is as effective as multiple *regular*-dose Crystalline penicillin and gentamicin as prophylaxis against puerperal infection in women undergoing elective caesarean section. It is therefore recommended for use as antibiotic prophylaxis in elective caesarean section.

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## LITERATURE REVIEW

### Introduction

Caesarean section is the surgical delivery, at term, of the baby via an incision through the abdominal and uterine walls. The origin of the term is obscure, including the most popular that Julius Caesar, the famous Roman emperor, was born this way. The most plausible is that it originated somewhere in the middle ages, from the Latin word caedere, which means 'to cut'(l)

Caesarean section is classified as either emergency or elective. An elective section is one that is performed before the onset of labour or before the appearance of any indications that might constitute an urgent indication(2).Indications for elective section may include previous caesarean section, a recurrent indication for the first section e.g. cephalo-pelvic disproportion, breech presentation, severe hypertensive disease, and prevention of mother-to-child transmission of H . I . V . }

### Risk Factors for post-partum infection

Post-partum Infectious morbidity is said to have occurred with findings of temperatures higher than 38°C on two separate occasions at least 24 hours apart following the first.24 hours aft£.r delivery, though overt infection may rarely occur without fever (3,4)

Post-partum infectious morbidity commonly takes the form of endometritis, urinary tract infections, pneumonia, or caesarean section wound infection. If untreated, these may progress to severe infection, e.g. septicaemia, septic pelvic thrombo-phrebitis, pelvic abscess, necrotizing fasciitis. Almost all post-partum infections are caused by bacteria normally present in the genital tract of pregnant women. The flora of the birth canal of pregnant women is essentially the same as that of non-pregnant womdn>About 70% of puerperal soft tissue infections are mixed infections consisting of both aerobic and anaerobic organisms. Although the organisms responsible for'puerperal infections vary considerably from hospital to hospital, wost puerperal infections are due to anaerobic streptococci,

gram-negative coliforms, bacteroides species and aerobic streptococci. Patterns of bacterial isolates in puerperal infections in particular hospitals are more important in guiding selection of antibiotics than are studies from literature (3,4).

Post-partum infectious morbidity affects 2-8% of pregnant women and is more common in women of low socio-economic status, premature rupture of the membranes, prolonged labour, multiple pelvic examinations and those who have undergone operative delivery (3,4). Wanjohi at Kenyatta National Hospital found as high and significant risk factors more than three vaginal examinations in labour, duration of operation more than 1 hour, nulliparity, no ANC received, ROM, duration of ROM exceeding 24hours, and unemployment) possibly as an indicator of low SES). Also found to be risk factors but not statistically significant were difficult operation, estimated blood loss at surgery of more than 1500mls, and a post-operative H.b less than lOg/dl (5). Kabare found as risk factors, duration of labour more than 12 hours, duration of ROM more than 12hours, emergency as opposed to elective caesarean*,section, and duration of caesarean section more than 1 hour. HIV sero-status had no influence on wound sepsis (6). There is however evidence that HIV positive CDC group III and IV patients have impairment of wound healing. HIV positivQ.patients who are otherwise well (group II) have similar outcome in terms of wound healing/septic complications as the HIV negative. (7,8). Pagyu P. et al carried.out a study on maternal complications in HIV infected women undergoing elective caesarean section in Thailand between 1999 and 2001. They found no statistically significant difference in maternal complications between the HIV infected and non-HIV infected women (9). Post-partum infectious morbidity is responsible for much of the morbidity associated with childbirth and contributes to the deaths of approximately 8% of all pregnant women who die each year. In the 2005 World Health Report, WHO lists infections as the second highest cause of maternal mortality, after hemorrhage, accounting for 15% of global maternal mortality (3,10). The single most important factor for post-partum maternal infection is Cesarean section delivery (3,11,12).

## Incidence

The incidence of post-partum infectious morbidity varies from institution to institution and is dependent majorly on the presence or absence of risk factors as well as use of prophylactic antibiotics. Goitom in Kenyatta National Hospital found rates of 18.9% to 40.6% among patients receiving cefuroxime and ampicillin respectively, in both emergency and elective caesarean sections (13 ).Kabare found 19% incidence of caesarean section wound infection at Kiambu District Hospital (both elective and emergency caesarean section). Wanjohi in Kenyatta National Hospital found wound infection rates of 13.3%, both elective and emergency caesarean sections. Maina C.K found a post caesarean section wound infection rate of 3.9% at Tenwek hospital (5,6,14).

## Aetiology

Goitom w at Kenyatta National Hospital found most puerperal infections (90%) to be caused by gram-negative organisms with e.coli being the commonest. This was in both emergency and elective caesarean sections. Sinei SK at Kenyatta *a'*

National Hospital found Klebsiella, e.coli and proteus as the most common isolates from the endocervix while staph aureus was the most common from abdominal wound infections (13,15).

In a recent study at Nazareth hospital, among patients undergoing elective caesarean section, Okiri L.A found e.coli to be the most prevalent organism, with others being klebsiella, proteus, pseudomonas and staphylococci. It is however noteworthy that though bacteria were isolated in 29 out of the 75 patients in the study, none had any clinical evidence of post-partum infectious morbidity and none needed treatment(16).

## Antibiotic Regimen

Goitom ,at Kenyatta National Hospital, compared the use of a five day course °f ampicillin to a single dose cefuroxime in both emergency and elective sections. He found that 40.6% of the ampicillin group and 18.9% of the cefuroxime group developed sepsis.

He however found that both drugs had similar efficacy when membranes were intact (RR2.93, 95%CI 0.93-9.23 p=0.427). Maina et al, in a clinical audit of post-caesarean wound infections at Tenwek hospital, and Okiri L.A in a study at Nazareth hospital, found no difference in septic complications between patients receiving either single-dose or multiple-dose ampicillin, gentamicin and metronidazole in both emergency and elective caesarean section and elective caesarean section respectively (13,14,16)

In a Cochrane database systematic review, Smaill F and Hofmeyr GJ reviewed eighty one trials comparing the use of antibiotics to no treatment in both emergency and elective caesarean section. They found that use of antibiotics in both substantially reduced the incidences of fever, endometritis, wound infection, urinary tract infection and serious infection.(11,12)

Bagratee et al in South Africa conducted a randomized clinical trial on 408 women undergoing elective caesarean section) and receiving either placebo or cefoxitin (one of only two second-generation cephalosporins with activity against Bacteroides and other gram-negative anaerobes). They found no significant difference in various outcome variables between the two groups (17).

Hopkins L et al, reviewed 51 trials of different regimens in a Cochrane database systematic review.Jhey concluded that both ampicillin and first generation cephalosporins have similar efficacy in reducing post-operative endometritis. There does not seem to-be any added advantage in utilizing a more broad-spectrum agent, like a second or third generation cephalosporin, or multiple dose regimens.(18).

Bacteriological sensitivity studies in Kenyatta National Hospital and Kenya in general have not been done regularly or routinely. It is however known that most puerperal infections are by gram-negative organisms and anaerobes. This regime covers both. Crystalline penicillin has good activity against gram positive organisms while gentamicin has good activity against gram- negative bacteria. Though gentamicin has poor activity against anaerobes on its own as it works by inhibiting protein synthg^is and its penetration through the cell membrane partly depends on oxygen-dependent active transport, it demonstrates good activity

against them when combined with penicillin and other antibiotics which inhibit cell-wall synthesis (2,20,21).

Aminoglycosides in general demonstrate concentration-dependent killing, i.e increasing concentrations of antibiotic kill an increasing proportion of bacteria and at a more rapid rate. Higher doses result in higher peak levels and better concentration-dependent killing, thus the choice of higher doses. Gentamicin also has good post-antibiotic effect i.e. the antibiotic effect persisting beyond the time during which measurable drug is present.(20,21). Gentamicin is both oto- and nephrotoxic especially when given for prolonged periods of time. In dosages of 3-7mg/kg, serum levels reach 3-8ug/ml. The dosages in this regime are within this safe range. Ototoxicity will result with serum levels exceeding lOug/ml, while levels for nephrotoxicity are higher (21,22).

## JUSTIFICATION AND UTILITY

At Kenyatta National Hospital and other public hospitals, X-pen plus gentamicin is the most commonly used antibiotic regimen in caesarean section. Despite this, no studies have been done on *s* efficacy. As presently used at KNH, it is a post-operative treatment regimen rather than pre-operative prophylaxis as it is given for three to five days. Anecdotal evidence exists in support of a single high dose x-pen plus gentamicin as prophylaxis m both emergency and elective caesarean sections. Bacterial resistance has been a rising problem in the studies done with penicillin and gentamicin, and as a principal, single-dose regimens help reduce continued exposure and development of resistance. This regime is the cheapest and most readily available in Kenyatta National Hospital and other public institutions. With the personnel constraints often found in public institutions, the single dose regimen, if effective,'could be adopted in other institutions where it v [w]ould be both time and cost saving.



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## RESEARCH QUESTION

Is a single high-dose of x-pen plus gentamicin as effective as a three day regular dose course of x-pen plus gentamicin as antibiotic prophylaxis during elective caesarean section?

## NULL HYPOTHESIS

A single high-dose of x-pen plus gentamicin is as effective as a three-day regular dose course of x-pen plus gentamicin as antibiotic prophylaxis during elective caesarean section.

## OBJECTIVES

### Broad objective

To compare the incidence of puerperal infection among patients receiving a single high-dose x-pen plus gentamicin with those getting multiple-dose x-pen plus gentamicin as antibiotic prophylaxis during-elective caesarean section at Kenyatta National Hospital.

### Specific objectives.

1. To compare the incidence of post-partum febrile illness among patients receiving a single high-dose x-pen plus gentamicin with those getting multiple-dose x-pen plus gentamicin as antibiotic prophylaxis during elective caesarean section at Kenyatta National Hospital.
2. To compare the incidence of post-partum clinical endometritis among patients receiving a single high-dose X-pen plus gentamicin with those getting multiple dose X?pen plus gentamicin as antibiotic prophylaxis during elective caesarean section at Kenyatta National Hospital.

3. To compare the incidence of surgical site (wound) infection among patients receiving single high-dose X-pen plus gentamicin with those getting multiple dose X-pen plus gentamicin as antibiotic prophylaxis during elective caesarean section at Kenyatta National Hospital.

## METHODOLOGY

### Study Area

This study was conducted at Kenyatta National Hospital, department of Obstetrics and Gynaecology. Kenyatta National Hospital is a national teaching and referral hospital located about three kilometers from the city centre. It has a bed capacity of about two thousand. The number of elective caesarean sections average twenty per week. The patients for elective section are booked from the ante-natal clinic and admitted to the maternity unit one day prior to surgery. They are usually given laboratory request forms for preoperative investigations i.e. hemoglobin estimation and renal function tests in the last ante-natal visit and report to the maternity unit with the results. For those without results, blood is drawn for the investigations on arrival at<the maternity unit. The elective caesarean sections in the hospital are done on Mondays, Wednesdays and Fridays by the senior registrar on duty. //

### Study population

The study population comprised women admitted for elective caesarean section at Kenyatta National Hospital maternity unit

### Study design

Ihis was a randomized doubi.e-blinded clinical trial. All women being admitted for elective caesarean section were interviewed (sequentially) by the chief •nvestigator or his trained assistant for recruitment into the study.

Those who declined recruitment from the start, those who did not meet the inclusion criteria and those who did not sign the informed consent form were excluded from the study.

For those who met the inclusion criteria and signed the informed consent, the first of three parts of a questionnaire was then filled. This part contained the baseline information about the patient e.g. socio-demographic data, ante-natal history, medical history and baseline investigation results.

Only women who still had none of the exclusion criteria by the time they got to theatre were randomized i.e if for example they ruptured membranes before the operation began, they were not randomized even though they had signed the informed consent (This was explained in the consent). When a woman entered theatre, she was randomized to one of the two arms (explained below). After the abdomen had been cleaned and draped, the anaesthetist administered the antibiotic as per randomization arm, 2megaupits of x-pen and 80 milligram of gentamicin for the multiple dose (the first dose of the multiple doses) and 4megaunits of x-pen and 240 milligrams of gentamicin for the single dose. This was done before the skin was incised. The operation then proceed as usual for the particular surgeon. At the end of the operation, the surgeon completed the second part of the questionnaire, which contained intra-operative details and prescribed antibiotics for continuation for the multiple dose patients. The third part of the questionnaire, which contained post-operative events was filled from the post-operative ward by the researcher or his assistant. The patient was examined daily for indicators of infection. These were vital signs (temperature, pulse rate, respiratory rate and blood pressure) twice daily in the morning and evening and the abdomen for the size of uterus, presence of tenderness and status of the incision wound. The lochia was also examined for amount, colour and smell. The abdomen and-status of lochia examination was done once daily. At two weeks post-operatively, afl,patients were examined for signs of wound sepsis and abnormal lochia by the chief investigator at the post-natal clinic.

Randomization

Seventy six sealed oblique envelopes each containing a card marked either SD (for Single Dose) or MD (for Multiple Dose) were shuffled and then numbered at random from 1 to 76 (38 for each arm of study). The insertion of the labelled cards into the opaque envelopes was done by the research assistant, then the numbering of the closed envelopes by the researcher to ensure blinding.

Before a woman entered theatre, the research assistant reviewed her to ascertain if she still met the inclusion criteria then opened an envelope (sequentially).He then wrote the allocated arm on the card on a sticker and stuck it on the top end of the questionnaire. The anaesthetist was then asked to administer the antibiotics as per the allocated arm. This was done before the incision on the skin.

Inclusion Criteria

i)Patients admitted for elective caesarean section at term.

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ii) Patients who gave informed consent to the study.

Exclusion Criteria

i)Patients who went into labour after admission (before getting to theatre).

ii)Patients who ruptured membranes before the operation began

inpatients who did not give informed consent

iv)Patients with deranged renal function tests

v)Patients with any known adverse drug reaction to any of the drugs to be used in the trial.

vi)Patients who were diabetic.

[v]ii)Patients with H.I.V/A.I.d!s clinical stage three or four as defined by WHO [c]'inical staging.

Outcome Variables

i) Post-partum febrile illness

ii)Surgical site (wound) infection

iii)Clinical endometritis

SAMPLE SIZE DETERMINATION

Sample size was calculated using the formulae below for superiority Randomized Clinical Trials (RTC), where single dose antibiotic was the Superior Treatment;

$$n = \frac{(P_0Q_0 + P1Q1)(Z\hat{}q/2 + Zrp)^2}{(p.-p.)^2}$$

Where;

n = Total required sample size for both the treatment units (patients), with equal cases (single dose) and controls (multiple dose);

Pi & $p_0$ = Prevalence of having Post-Partum infectious morbidity in cases and prevalence of post-partum infectious morbidity in controls respectively. ( At 18.9% and 40.6%) based on Goitom, KNH (6).

**Pi~Po** = expected differences^ the two treatment prevalence.

» ql =l-pl, qo=l-po.

Zra/2 = Probability of detecting a real difference between the two treatment groups in Comparison. (95%).

Zx-p = Probability of detecting a false difference in the two treatment groups (the power of test set at 80%)

Zra/2 & $Z_r$p are both cut off points along the x-axis of the standard normal probability distribution that represents probabilities matching the 95% confidence interval (1.96) and the statistical power of 80% (0.842), respectively.

Substituting the above values in the formulae above we get;

**n = 71.67**

**~ 72 Treatments**

Therefore, 36 were to be randomized to Single dose, and the 36 were randomized to multiple doses of Antibiotics.

Accounting for potential loss to follow-up and incomplete questionnaires of about 5%, a total of 76 questionnaires were'drafted.

**Data Collection**

**a) Instrument**

This was a quantitative coded, closed-ended questionnaire with different labeled sections.

**b) Examinations**

i)Temperature - This was taken from the axilla with a mercury thermometer-over a period of two minutes.

ii)Pulse rate - This was taken by palpation of the radial pulse over one minute

iii) Blood pressure - This was recorded from the left upper arm with a manual sphygmomanometer with the patient seated.

iv)Symphvsio-fundal height-This was taken with a tape-measure from the top of the pubic symphysis to the fundus of the uterus and related to 'fundal height' of a pregnant uterus.

**Study Limitations**

Blinding in this study was not possible after the randomization envelope was opened because after that, the woman and the researcher clearly knew which arm of treatment the woman was in. This however did not affect the results as the outcome variables were objectively me^sgr^ble.

Patients were initially supposed to be monitored for four days before discharge but this was not possible due to a change in policy with patients being discharged on the morning of the third day, thus they.did not complete all the multiple doses for the third day. No oral treatment was given upon discharge.

Data Analysis

Uncompleted questionnaires were kept under lock and key by the research assistant. Once complete, they were handed over to the researcher, who again kept them under lock and key till all the questionnaires were handed over.

Completed questionnaires were sorted out for completeness. Data was entered into the computer using Epi-info data entry programme by the researcher and a statistician. The data was then cleaned before analysis.

Analysis was done using SPSS-version 15.0 data analysis programme.

The data was presented in tables. Independent sample t-test was used to evaluate whether there was significant difference between the two treatment groups. Non- Parametric tests (Mann Whitney U test) was used to examine whether there was any significant finding between the two treatments e.g. age, while chi-square was used to establish the significant differences between the categorical variables among the treatment groups.

P-value of less than 5% ($P<0.05$) was considered statistically significant.

Ethical Considerations

i) Approval was sought from the University of Nairobi, department of Obstetrics and Gynaecology, and the KNH ethical and research committee.

ii) Informed consent was obtained from all the patients recruited for the study.

iii) Non consenting individuals were not hindered from obtaining appropriate management

RESULTS

Of the 76 questionnaires drafted, 75 were administered and only 72 were analysed, 36 for each arm of the study. Three patients, 2 from the multiple-dose arm and one from the single-dose arm, were not reviewed at the 2week post-operative clinic as they reported to have been out of reach, and although they reported no complications (on phone), their questionnaires were excluded as examination could not be done. There were 36 in each arm for the remaining 72.

Table 1: Socio-demographic Data characteristics of the study population* N=72)

| Characteristic | Regime | | |
|---|---|---|---|
| | Single Dose, N(%) | Multiple Dose, N(%) | p-value |
| Marital Status | | | |
| © Single | 5 (13.9) | 2(5.6) | |
| » Married | 30(83.3) | 34 (94.4) | 0.247 |
| • Separated | i *(iftj:* | 0 | |
| Level of Education | | | |
| © None | 0 | 0 | |
| * Primary | 5 (13.9) | 7 (19.4) | 0.241 |
| o Secondary | 24 (66.7) | 17(47.2) | |
| © Tertiary | 7 (19.4) | 12 (33.3) | |
| Occupation | *ft* | | |
| « Unemployed | 13(36.1) | 14 (38.9) | |
| o Formal Employment | 5(13.9) | 8(22.2) | 0.541 |
| © Business | 18 (50.0) | 14 (38.9) | |

There was no difference in the socio-demographic characteristics between the two groups. All women had some education, with majority in both arms having secondary education and above. Significant percentages in both arms were unemployed, 36.1% in the single and 38.9% in the multiple dose arms respectively.

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Table 2: Obstetric Characteristics of the study population (N=72)

| Characteristic | Regime | | p-value |
|---|---|---|---|
| | Single Dose, N(%) | Multiple Dose, N (%) | |
| Parity | | | |
| • Zero | 4 (11.1) | 3 (8.3) | 0.227 |
| ® 1 - 2 | 31 (86.1) | 28(77.8) | |
| ® >2 | 1(2.8) | 5 (13.9) | |
| Previous Scars | | | |
| ® None | 14 (38.9) | 11 (30.6) | 0.501 |
| * 1 to 2 | 21 (58.3) | 22 (61.1) | |
| • >2 | 1(2.8) | 3 (8.3) | |
| Indication for Current Section | | | 0.963 |
| ° 1 Previous Scar | 8 (22.2) | 10 (27.8) | |
| o 2 previous Scar | 11 (30.6) | 13(36.1) | |
| « 3 previous Scar | 1 (2.8)' | 2(5.6) | |
| • PMTCT | 9 (25.0) | 6(16.7) | |
| « Breech Presentation | 3 (8.3) | 2(5.6) | |
| * Other | 4 (11J.) | 3 (8.3) | |

There were no significant differences in obstetric characteristics- parity, number of previous scars or indication for the present section.

The majority of the women in both arms were either para one or two. The commonest indication for caesarean section was two previous caesarean sections.

Table 3: Pre-Operative Laboratory Profiles of the study population (N=72)

| Characteristic | Regime | | p-value |
|---|---|---|---|
| | Single Dose, N(%) | Multiple Dose, N (%) | |
| Hemoglobin(Hb) level | | | |
| « Hb<10 | 3 (8.3) | 3 (8.3) | 1.000 |
| • Hb> 10 | 33 (91.7) | 33 (91.7) | |
| HIV Status | | | |
| © +ve | 9(25.0) | 7 (19.4) | 0.571 ' |
| • -ve | 27 (75.0) | 29 (80.6) | |
| CD4 count (n=16) | | | |
| e <350 | 1 (11.1) | 2 (28.6) | |
| • 351-499 | 4 (44.4) | 2 (28.6) | 0.635 |
| • 500-999 | 4 (44.4)'. | 3(42.9) | |
| o >1000 | 0 | 0 | |

There was no difference in the pre-operative laboratory profiles. Three patients in each group had a haemoglobin level less than 10. 25% of the women in the single dose group were HIV positive compared to 19.4% in the multiple dose group.

**Table 4: Intra-operative events in the study population (N=72)**

| Characteristic | Regime | | |
|---|---|---|---|
| | **Single Dose, N(%)** | Multiple Dose, N (%) | p-va!ue j |
| **Type of Anaesthesia** | | | |
| • General | 12 (33.3) | 9 (25.0) | 0.437 |
| • Spinal | 24 (66.7) | 27 (75.0) | |
| **Abdominal Incision** | | | |
| • SUMI | 8(22.2) | 11 (30.6) | 0.422 \| |
| • Lower transverse | 28 (77.8) | 25 (69.4) | |
| **Intra-Operative Complications** | | | 0.348 |
| • None | 34 (94.4) | 36(100.0) | |
| • Difficult in Abdominal Entry | 1 (2.8) | 0 | |
| • Difficult Delivery of baby | . 1(2.8) | 0 | |
| **Blood Loss Mean (mis)** | 525.0 | 529.3 | 0.877 |
| **Duration of surgery Mean (minutes)** | • 48.4 | 49.4 | 0.553 **j** |
| **Suture type** | | | |
| • Absorbable | 33 (91.7) | 34 (94.4) | 0.643 j |
| • Non-absorbable | 3 (8.3) | 2(5.6) | |

Spinal anaesthesia was used in 66.7% of the patients in the single dose group and 75% in the multiple dose group. Majority of the patients had a lower transverse abdominal incision. Only 2 patients had intra-operative complications, 1 difficult abdominal entry (otherwise unspecified) and 1 difficult delivery of the baby (hydrocephalus). Absorbable sutures were used in over 90% of patients in both arms.

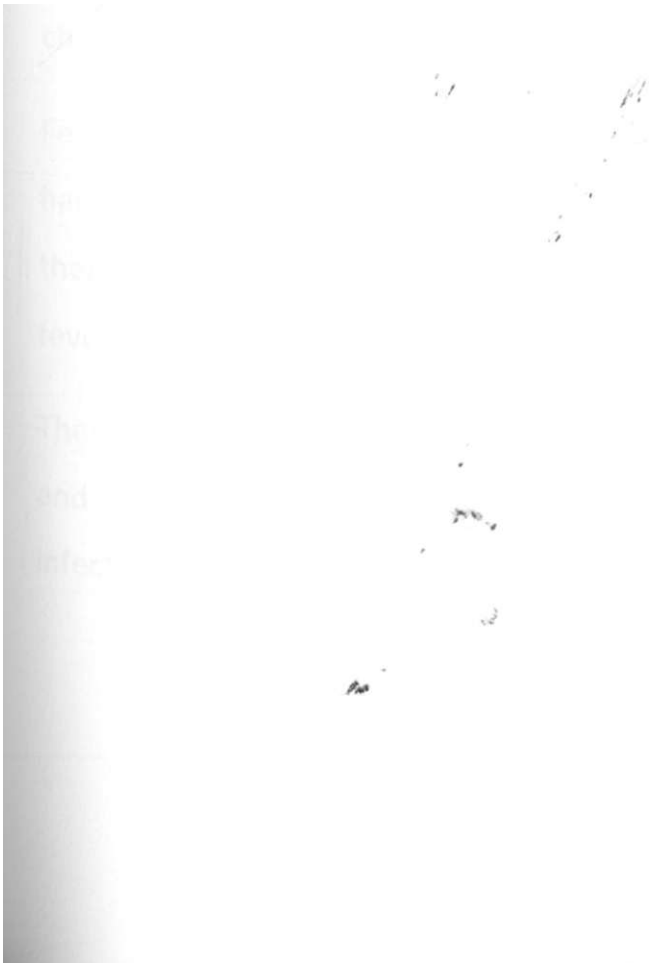
**Table 5: Clinical Indicators of Infection in the study population (N=72)**

| Indicator | Regime | | OR 95% a | p-va!ue j |
|---|---|---|---|---|
| | **Single Dose, N (%)** | Multiple Dose, , N(%) | | |
| **Fever** (> 38c) | 3 (8.3) | 3 (8.3) | 1.0 (0.2-5.3) | 1.000 |
| No Fever | 33 (91.7) | 33 (91.7) | | |
| **Wound Infection** | | | | |
| • Yes | 0 | 0 | - | - J |
| • No | 36 (100.0) | 36 (100.0) | | |
| **Uterine size (At 2wks post-op)** | | | | |
| • None | 35 (97.2) | 32 (88.9) | 0.2 (0.0 to 2.1) | 0.164 |
| • >12 weeks | 1 (2.8) | 4(11.1) | | |
| **Tenderness (At 2 weeks post-op)** | i | | | |
| • None | 21(61.8) | 25 (71.4) | 0.6 (0.2 to 1.8) | 0.395 |
| • Mild | 13 (38.2) | 10(28.6) | | |
| **Lochia Smell** | | | | |
| • Non-Foul | 36 (ioo:d) | 36 (100.0) | - | |
| • Foul | 0 (0.0) | (0.0) | | |
| **Lochia Color (At 2 Weeks ' post-op)** | | | | |
| • Rubra | 0 | 0 | - | 0.5435 |
| • Serosa | 0 | 1 (2.8) | | |
| • Alba | 16 (45.7) | 14 (38.9) | | |
| • No lochia | 19 (54.3) | 21 (58.3) | | |

Fever was recorded for 6 of the patients, 3 in each of the arms. These recordings were either on the first or seeopd post-operative day. None of these patients met the criteria for febrile illness *as defined.*There was no wound infection recorded in Patients in both arms at day 3 before discharge or at review on day 14. 4 patients had a uterine size corresponding to or above 12 weeks on review 2 weeks post-

operative. Significant numbers in both groups had lochia alba 2 weeks post-operatively. However, none had foul-smelling lochia.

*it'*



## DISCUSSION

Caesarean delivery is the biggest risk factor for post-partum infectious morbidity (3,11,12). Elective caesarean section is associated with much less post-operative infections than emergency caesarean section as it avoids the risk factors associated with labour, like ruptured membranes and pelvic examinations (3,4,5,6). A ntibiotic prophylaxis has however been shown to be beneficial in both elective and emcrgcncy caesarean sections (11,12).

The main finding in this study is that a single dose of prophylactic antibiotic given during elective caesarean section is as effective as multiple doses. Multiple studies, mainly done in the western world, have not demonstrated any advantage of multiple over single dose regimens, or of any drug regimen over others (18). Studies done locally, though few, have demonstrated similar findings (13,14,16). The regimen in this study was chosen as it met the criteria for an ideal prophylactic regimen (3,17), and is the mos,t .readily available, most utilized and cheapest in KNH and other public institutions in general.

Fever was the only noted adverse outcome. 6 patients, 3 (8.3%) in each group, had an episode of fever > 38°c in the first two days post-operatively. None of them however met the criteria for post-partum febrile illness *as defined* and the fever was easily controlled with anti-pyretics.

There was no observed wound infection in all patients in their stay in the ward and at 2 weeks post-operativgjy. The local studies that have recorded wound infections were mostly on both elective and emergency sections (5,6,13,14).

Though 5 women were found to have a uterine size at the level of 12 weeks, none were considered to have sub-involution. 3 of them (all in the multiple dose arm) had huge uterine fibroids, thus the apparent "sub-involution". The other two, one in each arm, were seen at 12 days post-operative, two days before the planned review. They had no fever, tenderness or any lochia and were not considered as having sub-involution. The two were reviewed one week later and found to have complete involution. In a similar study at Nazareth hospital in Kiambu, comprising 75 patients, Okiri L.A. compared the use of single dose Ampicilin, gentamicin and flagyl with multiple doses of the same and concluded they were equally effective. Fever was the main adverse outcome variable, recorded in 2.4% and 9.1% of the single and multiple dose groups respectively, with only one episode of fever recorded for all t^ patients (16). This was comparable to the findings of this study.

*I?'*

There is inconclusive evidence on the role of HIV infection in post-operative infectious morbidity, though there is evidence' however, that those HIV positive women in CDC stage 3 and 4 are at increased risk for post-operative wound infection (7,8). This study included only women in clinical stages 1 and 2. 16 patients (22.2%) in this study were HJV positive, 9 in the single dose and 7 in the multiple dose arms (p-value 0.571). Though none got post-operative infection, this proportion may be too small to draw conclusions from on the use of this regimen for prophylaxis in HIV infected women.

## CONCLUSIONS

- A single high dose of x-pen plus gentamicin is as effective a regimen for prophylaxis against post-operative infections after elective caesarean section as are multiple doses.

o It is inconclusive whether a single dose of x-pen plus gentamicin is effective for prophylaxis against post-operative infectious morbidity in HIV positive women undergoing elective caesarean section.

## RECOMMENDATIONS

« The use of single high dose Crystalline penicillin plus gentamicin for prophylaxis against post-operative infections during elective caesarean section at KNH.

» More studies on antibiotic prophylaxis in caesarean sections involving HIV positive women.

- More studies on the single dose x-pen plus gentamicin regimen to be conducted in other public institutions in other parts of the country. If similar results are obtained, they may inform policy on antibiotic prophylaxis during caesarean section in public institutions.

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Appendix 1: Questionnaire

Date;_____Study Number_

*Sociodemociraphic Data*

1. Age

2. Marital status [ ] l=single 2=married 3=separated 4= widowed

3. Level of Education | | l=none 2=primary 3=secondary 4=Tertiary

4. Occupation |___| l=Unemployed 2=Formal Employment 3=Business

*Obstetric History*

5. Parity j + ~

6. Gestation (Weeks) < > • >

7. Number of Previous Sections

8. Indication For Current Section

,/

*Pre-operative laboratory Profiles*

9-H.b. Q [ ~ ] g/dl

10. H.I.V Status | j l=Positive 2= Negative 3= unknown

11. CD4 Counts l=none 2=<350 3=351-499 4=500-999 4= > 1000

*j*

A*

*Intra-Operative Events*

13. Type Of Anaesthesia | j 1= General Anaethesia *2*- Spinal Anaesthesia

14. Abdominal Incision 1=S.U.M.I *2*- Lower transverse

15. Intra-Operational Complication^^ l=none

*2*- Difficult Abdominal Entry

3=Difficult Delivery of Baby

4=Difficult Achieving Hemostasis

5=Difficult Reversal of Anaesthesia

16. Estimated Blood Loss mis

t »

17. Duration of surgery ( From skin incision to' end of skin closure)

(Minutes) *<f'*

18. Suture Material Used For Skin Closure ' l=Absorbable 2=non-absorbable

An

*Post Operative Events*

*First post-operative day*

19. Vital signs Recordings

| | Morning | Evening |
|---|---|---|
| Temp (°c) | | |
| Pulse(beats/min) | | |
| Respiratory Rate(Breaths/min) | | |
| Blood Pressure(mmHg) | | |

20. State of Wound!"

l=Clean and dry

2-Sinus with sero-sanguineous fluid

3=Sinus with pus

4=Wound dehiscence

5=Burst abdomen

6=Other e.g. necrotizing fasciitis

21. State of uterus.

Symphysio-fundal height • Cms

Tenderness l=none 2=mild 3=moderate 4=severe

22. State of lochia .

Amount

l=mild 2=moderate 3=copious

Colour

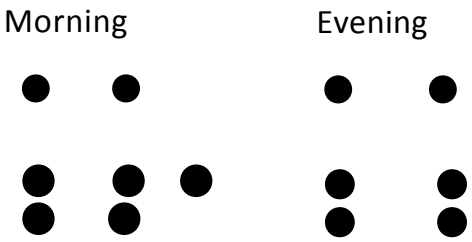
l=rubra 2=serosa 3=alba 4= other(specify) eg Green, yellow

Smell 1= Not foul 2=Foul

2.3)Other Physical findings (For Patients with Febrile Illness as defined)

*Second post-operative day*

24). Vital signs Recordings




Temp (°c)

Pulse(beats/min)

Respiratory Rate(Breaths/min)

Blood Pressure(mmHg)

25) State of Wound.T

l=Clean and dry

2=Sinus with sero-sanguineous fluid

3=Sinus with pus

4-Wound dehiscence

5=Burst abdomen

6=Other e.g. necrotizing fasciitis

26). State of uterus. .-v,

Symphysio-fundal height [Cms

Tenderness • | l=none 2=mild 3=moderate 4=severe



*v*

27). State of lochia .

Amount [___[ l=mild 2=moderate 3=copious

Colour 1___] l=rubra 2=serosa 3=alba 4= other(specify) eg Green, yellow

Smell 1= Not foul 2=Foul

28)Oth er Physical findings (For Patients with Febrile Illness as defined)

*Third post-operative day*

29). Vital signs Recordings

| | Morning | Evening |
|---|---|---|
| Temp (°c) | | |
| Pulse(beats/min) | | |
| Respiratory Rate(Breaths/min) | | |
| Blood Pressure(mmHg) | | |

30). State of Wound."

l=C!ean and dry

2=Sinus with sero-sanguineous fluid

3=Sinus with pus

4=Wound dehiscence

5=Burst abdomen

6=0ther e.g. necrotizing fasciitis

31). State of uterus.

Symphysio-fundal height [ [ 1 [Cms

Tenderness l=none 2=mild 3=moderate 4=severe

32). State of lochia .

Amount l=mild 2=moderate 3=copious

Colour l=rubra 2=serosa 3=alba 4= other(specify) eg Green, yellow

Smell 1= Not foul 2=Foul

33)Other Physical findings (For Patients with Febrile Illness as defined)

34) Other Investigations and'results ( For patients with febrile illness as defined)

i)FBC

ii)Urine c/s

iii)BS forMPs_____•

»

iv)Other

35). Bacteria Isolated

a) Wound | ] l=yes 2=no

b) Lochia | | l=yes 2=no

36). Bacteria type

a) Wound

b)Lochia

37). Sensitivity pattern

38). Discharged on_____post-operative day

*Post-natal visit (2 Weeks Post-op)*

39). State of Wound]

l=C!ean and dry

2=Sinus with sero-sanguineous fluid

3=Sinus with pus

4=Wound dehiscence

5=Burst abdomen

6=Other e.g. necrotizing fasciitis

40). State of uterus.

Symphysio-fundal height |__J | jCms

Tenderness F™] l=none 2=mild 3=moderate 4=severe

41). State of lochia .

Amount |___j l=mild 2=moderate 3=copious

Colour |____| l^rubra 2=serosa 3=alba 4= other(specify) eg Green, yellow

Smell l=non-foul 2=foul

42)Bacteria isolated

a)wound

b)Lochia (if abnormal lochia)

43).SensitivityPattern

Appendix *2:* Consent Form

I, Dr. M. Macharia, a post-graduate student in the department of Obstetrics and Gynaecology of the University of Nairobi, am conducting a study on antibiotic use in patients undergoing elective (planned) caesarean section at K.N.H. In this study, I will compare the use of a single dose of two commonly used antibiotics with that of a three day course of the same antibiotics. Their effectiveness will then be compared based on whether any infections develop or not. Studies, mostly done in western countries, have shown that giving antibiotics as a single dose before surgery is as effective in preventing development of infection as giving many doses. Some women will be given a single intravenous dose while others will receive additional doses for three days. The antibiotic regimen given to you will be determined by random selection and neither I nor you will know it before going to theatre. For those in whom infection will develop, appropriate treatment will be given as necessary. I will also need to tals specimens from your abdominal wound and a specimen from the vagina for investigations in the laboratory (if infection develops). This I will do on the day I notice signs of infection on the wound or an abnormal discharge from the vagina. If you develop a fever after the operation, I will need to do additional investigations to determine the cause. These may include blood tests, urine tests and x-rays.

Please note that if you go into labour or your membranes rupture before the operation begins, you will be excluded from the study.

Participation in this study is voluntary. You have a choice not to take part and this will not deny you getting the required medical attention. No financial or other kind of inducement will be given to anyone who chooses to take part. The results from this study may help improve quality of health care in K.N.H and the country in general. All information will be handled with utmost confidentiality and you will be entitled to information regarding-your treatment or the study at any time.

If you have any questions regarding the study, you can contact me through telephone number 0721-277938.

Your participation in the study will be highly appreciated.

L_____hereby voluntarily consent to participate in the study. I acknowledge that a thorough explanation of the nature and consequences of the study has been given to me by Dr/Mr./Mrs._____. I clearly understand that my participation is completely voluntary.

Signature_____Date

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November 9 2009

Dr. Martin Macharia
Dept. of Obs/Gynae
School of Medicine
University of Nairobi

Dear Dr. Macharia

RESEARCH PROPOSAL: "ANTIBIOTIC PROPHYLAXIS IN ELECTIVE CAESAREAN SECTION: SINGLE DOSE COMPARED TO MULTIPLE DOSE ANTIBIOTICS: A RANDOMIZED CLINICAL TRIAL" (P238/7/2009)

This is to inform you that the Kenyatta National Hospital/UON Ethics and Research Committee has reviewed and approved your above revised research proposal for the period 9th November, 20G9 - 8th November 2010. . < >

You will be required to request for a renewal of the approval if you intend to continue with the study beyond ihe deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

DR. L. W. MUCHIRI
AG SECRETARY, KNH/UQN-ERC

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