ORIGINAL ARTICLE

Single dose versus 24 hours antibiotic prophylaxis in caesarean delivery-an attempt to reduce antibiotic use

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Abstract:
Objective: To compare single dose antibiotic prophylaxis with 24 hour regime in Cesarean Delivery.
Study Design: Randomized Controlled Trial.
Setting and Duration: The study was conducted in Aga Khan Hospital for Women, Garden, Karachi, which is a secondary care unit of Aga Khan Hospital and Medical College Foundation from from April 2010 to November 2010.
Methodology: All eligible women, after taking informed consent, were randomized into two groups. Women in group A (n – 74) were given single dose antibiotic pre incision and in group B (n – 83) were given 24 hour antibiotic regime. All women were followed upto 30 days for infectious morbidity (SSI, fever, UTI and endometritis).
Results: Demographic, clinical and laboratory features were comparable among both the groups. In group A, 11 women (14.9%) and in group B, 17 women (20.5%) developed symptoms (p-value=0.35). According to CDC 1999 definition, Surgical site infection (SSI) was found in three women (4%) in group A and in 7 women (8.4%) in group B (p value=0.26). In group A, three women other than SSI required antibiotics (2 for UTI and 1 for Mastitis) compared to 1 (for Mastitis) in group B. Endometritis was not observed in any group.
Conclusion: Single dose antibiotic prophylaxis given pre incision was found to be effective in cesarean delivery. The risk of SSI was not increased, therefore antibiotic use can be reduced to single dose for prophylaxis in cesarean deliveries.

Key words: Antibiotic Prophylaxis, cesarean delivery, surgical site infection, infectious morbidity in cesarean section, antibiotic resistance, post surgery infection surveillance

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Introduction:

Mortality due to post operative infections markedly dropped down after the availability of antibiotics in mid 20th century. But surgical site infection (SSI) remains a global issue inspite of the use of variable regimes of antibiotic prophylaxis. In USA 2 to 5 percent of post operative patients develop SSI that accounts for 38 percent of nosocomial infections. [1, 2] In a Scottish surveillance of Healthcare Associated Infection Programme, SSI was recorded 11.2 percent[3]. Cesarean deliveries (CD) are more prone to develop SSI for the reasons of labor with or without ruptured membranes and many being carried in emergency situation[4]. In CD, overall SSI is reported 7.5 to 28.8 percent in emergency and 5.5 to 17.3 percent in elective cases. [5] Antibiotic prophylaxis is indicated in CD as it is classed in clean contaminated surgery with exposure to endogenous organisms gram –ve bacilli, group B streptococcus, enterococci and anaerobes as well as exogenous organisms i.e. staph. aureus.[6,7]

Injudicious use of antibiotics not only adds to financial burden, burden on hospital resources in terms of human resource, time and equipment, but also exposes women to undesirable side effects ranging from mild nausea and rash to severe life threatening drug reactions. More

over the antibiotics compromise immunity, suppress host defenses and subject to further risk of acquiring infections. The most alarming element is the emergence of resistant strains and multidrug resistant infections. [8-11] Hence serious efforts should be made to minimize the use of antibiotics.

In our hospital practice of antibiotic prophylaxis in CD was preoperative followed by 24 hour postoperative antibiotics (second generation Cephalosporin with Metronidazole). Antibiotic has not been recommended to sterilize tissue but to decrease contamination to the level that can be handled by the host defenses. There was ample evidence of safety of single dose prophylaxis in literature [5, 12]. So we considered to conduct a study, in our setting, to test single dose regime against the implemented one. The purpose was to further reduce antibiotic usage and develop best guideline for antibiotic prophylaxis in CD for our setup.

Methodology:

It was presumed that introduction of single dose antibiotic prophylaxis in CD, in our setting, will not increase SSI and other infectious morbidity. The study was conducted in Aga Khan Hospital for Women, Garden, Karachi, which is a secondary care unit of Aga Khan Hospital and Medical College Foundation. The duration of study was from April 2010 to November 2010. It was a randomized controlled trial.

Inclusion criteria: Women undergoing emergency or elective CD who consented to be included in the study.

Exclusion criteria: Women having absent membranes for more than 4 hours, clinical or laboratory evidence of existing infection, hemoglobin less than 8 g/dl, uncontrolled diabetes or known case of suppressed immunity were excluded from the study.

Procedure: Approval of the study was taken from Ethical Review Committee of Aga Khan University and informed consent was taken from all women. The women were randomized by picking sealed opaque envelope, into two groups. 178 women consented for study inclusion. 6 were not recruited due to breach of protocol. 15 women were removed from the study, due to need for further antibiotics within 24 hours of recruitment (figure 1). Women in group A (n – 74) were given single dose of antibiotics within half an hour of giving incision. In group B (n- 83) additional three doses were given in 24 hours post operative. Two antibiotics that were already in practice were used: - Amoxicillin + Clauvenic acid 1.2 g i/v. - 2nd generation Cephalosporin (Cefuroxime) 1.5 g i/v + Metronidazole 500 mg i/v.

98% of caesarean deliveries were performed under spinal anesthesia. They were allowed per oral within 6 hours, mobilized within bed soon after surgery and out of bed within 12 hours. Urinary catheter was removed within 12-20 hours. Dressing was removed in 36-48 hours followed by bath. Hemoglobin level was checked on second post operative day and anemia if detected, treated accordingly. Education regarding nutrition, hygiene and wound care was given to all. The women were discharged on third post operative day with verbal and written advice to report if sign or symptom of infection developed. They were called for follow up and stitch removal (subcutaneous prolene 1) on seventh to eighth post operative day. (surveillance for infectious morbidity was done up to 30 days after

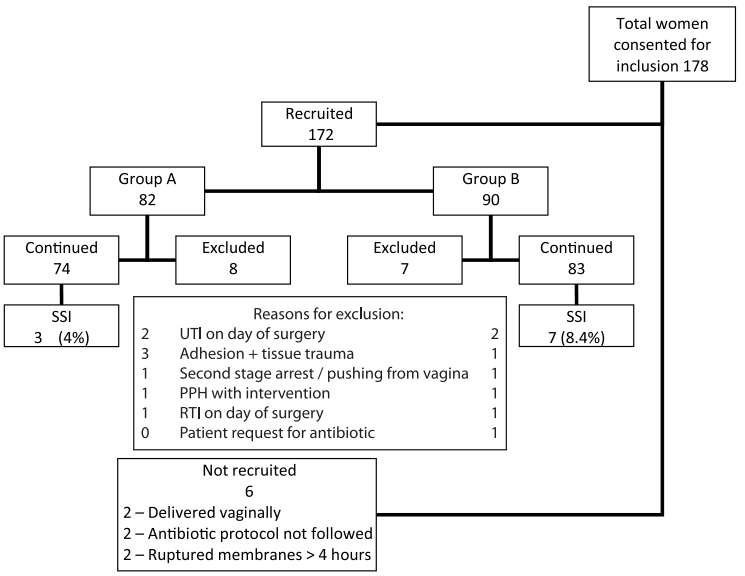

Figure 1:

surgery, as follows:

- Direct observation during 72 hours of hospitalization.
- Verbal enquiry and direct observation on follow up on 7th to 8th post operative day.
- Verbal enquiry after day 30.

Surveillance was done for fever >38 °C, wound erythma induration with pain, wound discharge or dehiscence, foul discharge per vaginum. All women with signs and symptoms reported in the clinic. SSI was defined and classified according to CDC 1999 guideline. [12]

All analyses were conducted by using the Statistical Package for Social Science SPSS (Release 19.0, standard version, copyright © SPSS; 1989-02). All p-values were two sided and considered as statistically significant if < 0.05. A descriptive analysis was done by comparing women baseline status of single dose versus 24 hour regime for demographic and baseline symptom features and results are presented as mean ± standard deviation for quantitative variables and number (Percentage) for qualitative variables. Baseline characteristics were compared between the two groups for each of the study medication regime using independent sample t-test for continuous data and chi-square or Fisher exact test for categorical data.

Results:

A total of 74 women in group A received single dose antibiotic and 83 women in group B received 24 hour regime. Demographic, clinical and laboratory features were comparable among both the groups(Table 1). ugh Elective CD was performed in less women in group A, 35(47.3%) compared to 52(62.7%) women in group B, but the difference was not significant (p value=0.053). Table 2 reflects the number of women with symptoms in each group. Most of the women had more than one symptom. Febrile illness was seen in 5 women (6.6%) in group A. Of these 1 had SSI, 1 had urinary tract infection (UTI) and 1 had Mastitis, whereas in the remaining 2 women fever settled on simple antipyretics. In group B, 3 women (3.6%) had fever, of which 2 had SSI and 1 had Mastitis. Erythma and induration was seen in 6 women (8.1%) in group A and in 7 women (8.4%) in group B. Wound discharge occurred in 2 women (2.7%) in group A and 11 women (13.3%) in group B of which 5 women had serous discharge that was self limiting and did not require any treatment. There was no wound dehiscence in group A unlike 4 women (4.8%) with dehiscence in group B. Most of the symptoms appeared after discharge of the women and within 8 to 10 days.

Summary of infectious morbidity is given in Table 3. In group A, 11 women (14.9%) and in group B, 17 women (20.5%) developed symptoms (p-value 0.35). According to CDC 1999 definition, SSI was seen in 3 women (4 %) in group A and 7 women (8.4%) in group B (p value=0.26). 3 women other than SSI, in group A required antibiotics (2 UTI, 1 Mastitis) compared to 1 (Mastitis) in group B. Endometritis was not observed in any group. The most commonly used prophylactic antibiotic was Amoxicillin + Clauvenic acid in both the groups. Level of experience of the surgeon did not make any difference.

Discussion:

The results of our study showed that reducing antibiotic to pre incision single dose regime was safe and did not increase SSI in CD in our setup. SSI was less in group A, 3% versus 8.4% though not statistically significant. CD rates are reported to be around 30% in the developed world, reaching upto 50% in some developing countries and is on the rise worldwide. [13, 14] SSI, fever, UTI and endometritis are known postpartum infections after CD and the burden is increasing with the rise in CD. Lamont (2011) quoted the prevalence of SSI in 10%, fever 15% and UTI 10% in CD inspite of antibiotic prophylaxis and the prevalence was 50% higher in emergency cases.[5] National Nosocomial Infection Surveillance (NNIS) 1998 reported SSI rate in CD 3.3 % to 4.4 % in USA hospitals.[15]

Two main factors that determine SSI are surgical techniques (including standard infection control practices) and antibiotic prophylaxis, in clean and clean contaminated cases. Burke

Table 1: *Demographic, baseline clinical and laboratory features*

Variable	Group A	Group B	P – value
Mean Age - Years(SD)	26.6 (4.5)	27.66 (5.2)	0.18
Mean BMI - (SD)	27.9 (5.2)	29.0 (5.3)	0.02
Socioeconomic status - n (%)			
Poor/lower middle	44 (59.5)	54 (65.1)	
High/upper middle	30 (40.5)	29 (34.9)	0.46
Education level - n (%)			
Up to primary	8 (10.8)	8 (9.6)	
Secondary and above	66 (89.2)	75 (90.4)	0.91
Parity - n (%)			
Primigravida	25(33.8)	24(28.9)	
Multigravida	45(60.8)	54(65.1)	
Grand Multigavida	4(5.4)	5(6.0)	0.80
Elective LSCS - n (%)	35(47.3)	52(62.7)	
Emergency LSCS - n (%)	39(52.7)	31(37.3)	0.053
Mean duration of Labor - (min)	398.3	362.9	0.44
Mean duration of ruptured membranes - (min)	137.1	120.0	0.5
No. of vaginal examinations	3.0	3.3	0.36
hemoglobin at delivery			
8 - 10.4 g/dl	22(29.7) g/dl	16 (19.3)g/dl	
10.5 g/dl and above	52(70.3) g/dl	67(80.7) g/dl	0.27 g/dl

Table 2: *Description of Individual Symptoms*

Morbidity Symptoms	Group A n=74 (%)	Group B n=83 (%)
Fever (n)	5 (6.6)	3 (3.6)
Erythma / Induration (n)	6 (8.1)	7 (8.4)
Wound discharge (n)	2 (2.7)	11 (13.3)
Wound Dehiscence (n)	0 (0)	4 (4.8)
+ve wound culture (n)	1 (1.4)	3 (3.6)

Table 3: *Analysis of Infectious Morbidity*

	Group A n = 74	Group B N = 83	p – value
Subjects with symptoms - n(%)	11(14.9)	17 (20.5)	0.35
Symptoms settling without Antibiotics - n(%)	5 (6.8)	9 (10.8)	0.69
Surgical Site Infection - n(%)	3 (4.05)	7 (8.4)	0.26
Other infections requiring antibiotics - n (%)	3 (4.05)	1 (1.2)	
UTI	2	0	
Mastitis	1	1	
Endometritis	0	0	

introduced the practice of antibiotic prophylaxis in 1960.[16] This has greatly evolved in the last 20 years.[7] There is large variation in practice regarding choice of drug, timing and duration of antibiotic prophylaxis. These have largely been addressed. CDC guideline 1999 defines the preventive actions for infection control in surgical cases. Antibiotic prophylaxis in CD has proved to be beneficial and reduces the risk of infectious morbidity by 50% - 70%. The benefit is both in high risk cases (labor and ruptured membranes) and in low risk cases (no labor and intact membranes).[17-19] SSI was more in women with elective delivery in our study and according to literature also, elective delivery confers no protection against infectious morbidity. [20]

Pre incision antibiotic administration is found to be better than during and after surgery. The idea is to attain maximum concentration of antibiotic at the time of contamination (surgery). Exception to this rule is made for CD where administration of antibiotic prophylaxis is recommended immediately after cord clamping for protection of the neonate. [12, 21, 22] Concerns have been raised of neonatal sepsis being masked or increased susceptibility to allergies and asthma due to induction of abnormal gut colonization by antibiotics. On the other hand, many studies have shown that not giving antibiotics pre incision increases the chances of post partum maternal infection without conferring any benefit to the neonate. Although American Academy of Pediatricians (AAP) guideline recommend pre incision prophylaxis, these studies should be tempered cautiously till more evidence is available. [17, 23, 24]

Choice of antibiotics should be according to susceptible organisms and most of the guidelines recommend narrow spectrum antibiotics (ampicillin, first generation cephalosporin), to contain cost and to prevent emergence of resistant strains. These are as effective as broad spectrum antibiotics for prophylaxis. [25] Swedish Norwegian consensus conference for antibiotic prophylaxis in 1998 recommended reducing antibiotics given for prophylaxis, to single dose first or second generation cephalosporins with or without Metronidazole. [26]

As the practices and guidelines have evolved over the years, duration of antibiotic prophylaxis has been reduced from days to 24 hours, further to single dose. Additional doses post operative

do not confer additional benefit.[6, 12] In our study, 24 hour regime group had more SSI than single dose group (8.3% vs 4%). Three studies by Kausar R, Ambreen T, and Wali A also showed that excessive and prolonged use of antibiotics did not give any protection against infection.[27-29] Suppression of host defenses by extended use of antibiotics may increase susceptibility to infections.

Indiscriminate use of antibiotics, emergence of resistant flora and its associated dire consequences are now globally recognized and duly addressed. Implementation of standard guideline for infection control including those for antibiotic prophylaxis is the answer. Only this can reduce wide variation in practices and induce confidence for curtailing unnecessary antibiotic. The same concern was shown by SM Wild regarding varied practice of antibiotic use in CD and need for guideline in UK hospitals. 20 Resistance to change practices is always encountered. Tippawan observed that older faculty had tendency to give more doses especially in cases of labor, ruptured membrane and repeated vaginal examination.[30] However it is also important to identify additional risk factors e.g. rupture membranes for >6 hrs, underlying Bacterial Vaginosis and other infections, uncontrolled diabetes, morbid obesity, etc. to extend antibiotic prophylaxis as required. [31] Adherence to standard infection control practices perioperatively is mandatory in order to practice single dose antibiotic regime for prophylaxis successfully. Post discharge surveillance is an important activity in strategy for infection control as 70-80% of infections occur after discharge. [3, 32, 33] This was seen in our study where most symptoms appeared after discharge and with in 8 to 10 days. In this study 2 women in group A had UTI versus none in group B. Prolonged retention of Foley's catheter after surgery may have contributed to uncomplicated urinary tract infection. Practices such as prolonged postoperative catheterization and intravenous canula site placements contribute significantly to postoperative febrile morbidity and need to be evaluated to allow success for single dose therapy to be of benefit. This needs further evaluation.

Conclusion:

In routine cases of cesarean delivery, elective as well as emergency, single dose regime of antibiotic given pre incision was effective. The risk of SSI was not increased while cost and the adverse effects of additional antibiotics were reduced. The practice of single dose antibiotic prophylaxis is an important step to fight against antimicrobial resistance. Extended antibiotic prophylaxis can be considered in cases with additional risk factors for SSI.

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