Randomised Study to Compare the Incidence of Postoperative Infection Following Timing of Prophylactic Antibiotics at Elective Caesarean Section

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Abstract

Objective: To Compare the incidence of postoperative infection following timing of prophylactic antibiotics at elective caesarean section.

Study Design: A double blinded randomized controlled trial.

Patients and Methods: Patients were classified into two groups: Group1: 100 patients given antibiotic 15-30 minutes before skin incision. Group 2: 100 patients given antibiotic just after cord clamping.

Results: There was no significant difference between both groups regarding maternal age, gestational age, indications for cesarean section, hospital stay, postoperative pyrexia, wound infection, endometritis, urinary tract infections or laboratory data.

Conclusions: The results of the current study showed that the usage of prophylactic antibiotics before skin incision and its usage just after cord clamping are equally effective in preventing postoperative infective complications.

Key Words: Post operative – Infection – Timing – Prophylactic antibiotics – Cesarean section.

Introduction

CESAREAN delivery is the most common major surgical procedure in the United States and elsewhere [1]. The useful effect of prophylactic antibiotics in reducing the occurrence of infectious morbidity from caesarean section, whether elective or emergency, is well confirmed [2].

A single dose of first-generation cephalosporin is as effective as multiple doses of broad-spectrum agents [3]. The effectiveness of prophylactic antibiotics depends on their presence in effective concentrations throughout the operative period [4].

Women undergoing cesarean section are at 5- to 20-fold more risk of infection than are women delivering vaginally. Infectious complications after cesarean delivery are an important cause of maternal morbidity, and can prolong the period of hospital stay. These include: Wound infection, postpartum endometritis, and urinary tract infection [5,6].

Antibiotic prophylaxis is recommended for all women undergoing caesarean section as routine use of prophylactic antibiotics reduces the risk of post-caesarean infections by over 50% from baseline rates which are as high as 20-50% [7].

Patients and Methods

A double blinded randomized controlled trial was conducted at the Department of Obstetrics and Gynecology, Kasr El-Aini Teaching Hospital, Faculty of Medicine, Cairo University, Cairo, Egypt, between January 1st and June 30, 2014. The study protocol was approved by the Scientific Research Committee of the department. Pregnant women with indication for cesarean section were enrolled after providing informed consent. Elective cesarean section is defined as cesarean performed before the presence of labor.

Inclusion criteria:
- Women undergoing elective cesarean section.
- Pregnant at term.

Exclusion criteria:
- Fever on admission.
- Gestational age less than 37 weeks.
- Using of antibiotics during the last 24 hours.
- Abnormally adherent placenta (accreta, increta or percreta).

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- Suspected chorioamnionitis.
- Emergency caesarean section.
- Rupture membranes more than 12 hours.
- Bleeding diathesis.
- Previous history of postpartum hemorrhage.
- Multiple pregnancy.
- High risk pregnancy (gestational diabetes or severe preeclampsia).

Randomization done by computer generated random number in sealed opaque envelopes. Each patient was given a study information sheet and a consent was signed. Sample size was calculated to prevent type II error. Based on these data, we would need to study 100 cases in each arm to be able to reject the null hypothesis that the rates for the experimental and control groups are equal with a probability of 80%. The type I error probability associated with this test for the null hypothesis is 0.05. We used an uncorrected chi-squared statistic to evaluate this null hypothesis.

200 pregnant women with an indication for caesarean section were randomly allocated. The patients were randomly distributed using random number tables and the treatment allocation was done using closed opaque sealed envelope by an assigned nurse just before the caesarean section. The patient and the investigators who follow-up the patient were blinded to allocation to avoid bias.

Patients were classified into two groups:
Group 1: 100 patients given antibiotic before skin incision.
Group 2: 100 patients given antibiotic just after cord clamping.

Ceftriaxon (Oframax; Ranbaxy, Egypt) 2gm I.V., (15-30 minutes) preoperative.
Or Ceftriaxon (Oframax; Ranbaxy, Egypt) 2gm I.V., (15-30 minutes) just after cord clamping.

A preoperative prerequisite testing hypersensitivity against cephalosporins was done. Hypersensitive cases were excluded from study.

Women’s age and obstetric history were recorded. Significant findings in the history were registered eg, hypertension, urinary tract infection and drug intake eg,antibiotics and corticosteroids.

General and obstetric examinations were done for all women included.

Complete blood count was done for all women from which hemoglobin and total leucocytic counts were recorded.

All operations were performed with regional anesthesia; spinal anesthesia performed with a 27G needle, using 12mg of 0.5% hyperbaric bupivacaine associated with 25ug fentanyl. No vasoconstrictor was used routinely, apart from ephedrine (10mg) if blood pressure decreased 20% from baseline values.

Cesarean deliveries were performed by third-year obstetric residents, under the guidance of staff obstetricians.

Operation under spinal anesthesia, using following precautions:
- Shaving lower abdominal and suprapubic hair.
- Insertion of Folley’s catheter.
- Scrubbing of the skin with antiseptic solution (usually Betadine).
- Skin incision by Pfannensteil incision.
- Opening of subcutaneous tissue.
- Opening of rectus sheath by transverse incision.
- Separation of recti muscles.
- Good exposure of lower uterine segment to be opened by C-shaped incision.
- Fetal delivery and cord clamping.
- Complete delivery of placenta & cord.
- Uterine closure in two layers with Vicryl 1 sutures & ensure good hemostasis (insitu closure).
- Approximation of recti & Closure of sheath by vicryl sutures.
- Closure of subcutaneous fat if more than 2cm.
- Subcuticular skin closure.
- Covering the suture line with sterile pad & clean dressing done on the morning of the day after.
- Follow-up of the patient as long as she is hospitalized & discharged after confirmed positive intestinal motility and passage of flatus.

Additional oxytocic therapy used if inadequate uterine tone present. The volume of blood loss during cesarean section and in the first hour post operatively was assessed in a standard manner.

Vital signs monitored continuously during surgery and every 30 minutes thereafter until transfer to the postpartum ward.

Postoperative care: Vital signs every 4 hours, removal of catheter and advancement of diet on the first postoperative day.

For postoperative analgesia, all patients were administered one ampoule Diclofenac sodium 75mg (Voltaren; Novartis, Egypt) intravenous infusion.
on dextrose solution followed by Diclofenac potassium 50mg (Cataflam; Novartis, Egypt) tablet every 8 hours for until no longer needed.

The intravenous dextrose infusion was administered for 24 hours. During the first 12 postoperative hours the patients were allowed minimal water intake by mouth. Liquids and soft foods were allowed only after intestinal sounds were heard and a normal diet only after the first flatus.

A diagnosis of endometritis was established when the body temperature exceeded 38.5°C twice, 6 hours apart, and was accompanied by tenderness of the uterus, foul smelly discharge, tachycardia and leukocytosis (white cell count more than 15,000/ml) [8].

Febrile morbidity means persistent fever of at least 38°C for at least 24 hours after surgery not associated with infection elsewhere [5].

Wound infections were characterised by the presence of purulent discharge, erythema more than 1cm and induration of the incision site [6].

A diagnosis of urinary tract infection was only considered when urinary symptoms (maternal temperature, flank pain), associated with significant bacteriuria (>1,000,000 organisms/ml) on culture of mid-stream specimen of urine were noted [5].

The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Science) software version 15. The statistical analysis was performed using X² test, odd ratios, and 95% confidence intervals. The level of significance was taken at p-value <0.05 is significant, otherwise is non-significant.

Good Clinical Practice (GCP):

The procedures set out in this study, pertaining to the conduct, evaluation and documentation of this study, were designed to ensure that the investigators apply the principles of good clinical practice and the ethical principles laid down in the current revision of the Declaration of Helsinki.

Results

A double blinded randomized controlled trial was conducted at the Department of Obstetrics and Gynecology, Kasr El-Aini Teaching Hospital, Faculty of Medicine, Cairo University, Cairo, Egypt, between January 1st and June 30, 2014.

Patients were classified into two groups:

Group 1: 100 patients given antibiotic before skin incision.

Group 2: 100 patients given antibiotic just after cord clamping.

Ceftriaxon (Oframax; Ranbaxy, Egypt) 2gm I.V., (15-30 minutes) preoperative.

Or Ceftriaxon (Oframax; Ranbaxy, Egypt) 2gm I.V., (15-30 minutes) just after cord clamping.

Table (1): Comparison between both groups as regards maternal age.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A (100)</th>
<th>Group B (100)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52 (52%)</td>
<td>61 (61%)</td>
<td></td>
</tr>
<tr>
<td>Less than 25</td>
<td>27 (27%)</td>
<td>22 (22%)</td>
<td>More than 0.05</td>
</tr>
<tr>
<td>26-30</td>
<td>21 (21%)</td>
<td>17 (17%)</td>
<td>NS</td>
</tr>
<tr>
<td>More than 30</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table (1) shows no statistically significant difference between both groups regarding age.

Table (2): Comparison between both groups as regards gestational age.

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Group A (100)</th>
<th>Group B (100)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>39.9±0.8</td>
<td>39.8±0.8</td>
<td>More than 0.05</td>
</tr>
</tbody>
</table>

Table (2) shows no statistically significant difference between both groups regarding gestational age.

Table (3): Comparison between both groups as regards indications of Cesarean section.

<table>
<thead>
<tr>
<th>Indications</th>
<th>Group A (100)</th>
<th>Group B (100)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous CS</td>
<td>18 (18%)</td>
<td>21 (21%)</td>
<td></td>
</tr>
<tr>
<td>Bad obstetric history</td>
<td>7 (7%)</td>
<td>9 (9%)</td>
<td></td>
</tr>
<tr>
<td>Breech</td>
<td>7 (7%)</td>
<td>8 (8%)</td>
<td></td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>3 (3%)</td>
<td>3 (3%)</td>
<td>More than 0.05</td>
</tr>
<tr>
<td>Post dates</td>
<td>17 (17%)</td>
<td>16 (16%)</td>
<td>NS</td>
</tr>
<tr>
<td>Elderly primigravida</td>
<td>15 (15%)</td>
<td>15 (15%)</td>
<td></td>
</tr>
<tr>
<td>Failed induction</td>
<td>10 (10%)</td>
<td>8 (8%)</td>
<td></td>
</tr>
<tr>
<td>Cephalopelvic disproportion</td>
<td>6 (6%)</td>
<td>5 (5%)</td>
<td></td>
</tr>
<tr>
<td>Macrosomia</td>
<td>8 (8%)</td>
<td>6 (6%)</td>
<td></td>
</tr>
<tr>
<td>Twins</td>
<td>9 (9%)</td>
<td>9 (9%)</td>
<td></td>
</tr>
</tbody>
</table>

Table (3) shows no statistically significant difference between both groups regarding indications for Cesarean section.
Table (4): Comparison between both groups as regards hospital stay.

<table>
<thead>
<tr>
<th>Hospital stay (days)</th>
<th>Group A (100)</th>
<th>Group B (100)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>5.2±1.7</td>
<td>5.3±1.6</td>
<td>More than 0.05 NS</td>
</tr>
</tbody>
</table>

Table (4) shows no statistically significant difference between both groups regarding hospital stay.

Table (5): Comparison between both groups as regards post-operative pyrexia.

<table>
<thead>
<tr>
<th>Pyrexia</th>
<th>Group A (100)</th>
<th>Group B (100)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (6%)</td>
<td>7 (7%)</td>
<td>More than 0.05 NS</td>
<td></td>
</tr>
</tbody>
</table>

Table (5) shows no statistically significant difference between both groups regarding post-operative pyrexia.

Table (6): Comparison between both groups as regards post-operative wound infection.

<table>
<thead>
<tr>
<th>Wound infection</th>
<th>Group A (100)</th>
<th>Group B (100)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 (5%)</td>
<td>7 (7%)</td>
<td>More than 0.05 NS</td>
<td></td>
</tr>
</tbody>
</table>

Table (6) shows no statistically significant difference between both groups regarding post-operative wound infection.

Table (7): Comparison between both groups as regards post-operative endometritis.

<table>
<thead>
<tr>
<th>Endometritis</th>
<th>Group A (100)</th>
<th>Group B (100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>97 (97%)</td>
<td>96 (96%)</td>
</tr>
<tr>
<td>Yes</td>
<td>3 (3%)</td>
<td>4 (4%)</td>
</tr>
</tbody>
</table>

Table (7) shows that no difference in both groups regarding post-operative endometritis.

Table (8): Comparison between both groups as regards post-operative urinary tract infections.

<table>
<thead>
<tr>
<th>UTI</th>
<th>Group A (100)</th>
<th>Group B (100)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (6%)</td>
<td>6 (6%)</td>
<td>More than 0.05 NS</td>
<td></td>
</tr>
</tbody>
</table>

Table (8) shows no statistically significant difference between both groups regarding postoperative pyrexia.

Table (9): Comparison between both groups as regards laboratory data.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A (100)</th>
<th>Group B (100)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>11.8±2</td>
<td>12±1</td>
<td>More than 0.05 NS</td>
</tr>
<tr>
<td>WBCs</td>
<td>9±1.2</td>
<td>8.5±1.3</td>
<td>More than 0.05 NS</td>
</tr>
<tr>
<td>Platelets</td>
<td>235±55</td>
<td>216±59</td>
<td>More than 0.05 NS</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>0.6±0.03</td>
<td>0.7±0.02</td>
<td>More than 0.05 NS</td>
</tr>
</tbody>
</table>

Table (9) shows no statistically significant difference between both groups regarding laboratory data.

**Discussion**

Cesarean section in the absence of labor is performed for many indications, including breech presentation, placenta previa and most frequently for having had a prior cesarean delivery [8]. Likewise, in the current study, previous cesarean section constituted the most frequent indication of elective cesarean section.

In a revised meta-analysis [9], the use of prophylactic antibiotics was shown to decrease the risk of both postoperative fever and endometritis. In the current study, proper preparation of the skin and incision site was performed using Betadine surgical antiseptic solution in addition to the adherence to the regular theater aseptic and antiseptic regulations.

There was no significant difference between both groups regarding maternal age, gestational age, indications for cesarean section, hospital stay, postoperative pyrexia, wound infection, endometritis, urinary tract infections or laboratory data.

The findings are consistent with the conclusion of Thigpen et al., [10] who found that there was no difference in maternal infectious morbidity whether antibiotics were given before skin incision or after cord clamping.

Yildrim et al., [11] found that time of antibiotic prophylaxis application does not change maternal infectious morbidity in cesarean section deliveries. Wax et al., Gordon et al., and Cunningham et al., [12-14] found similar infectious morbidity between both groups.
Macones et al. [18] showed that either preoperative antibiotic therapy or antibiotic administration after cord clamping is a reasonable clinical method for reducing postcesarean infectious morbidity.

Mohamed Kandil et al. [16] showed that Prophylactic antibiotic administration either prior to surgery or after cord clamping is probably equally effective in reducing the Postoperative infectious morbidity after Cesarean in low resource settings.

S. Kalaranjini et al. [17] found that timing of administration of prophylactic antibiotics for elective caesarean section either before skin incision or after cord clamping did not have significant difference in the occurrence of post-operative infectious morbidity. No adverse neonatal outcome was observed in women who received the antibiotic before skin incision.

Bashier Osman et al. [18] found that there was no difference in the two regimens (pre-incision or post-clamping of the umbilical cord) of ceftizoxime as prophylactic for elective cesarean delivery.

In contrast to our study, Sullivan et al. [19] and Costantine et al. [20], found that there is strong evidence that antibiotic prophylaxis for cesarean delivery that is given before skin incision, rather than after cord clamping, decreases the incidence of post partum endometritis and total infectious morbidities without affecting neonatal outcomes.

This may be due to use of different antibiotic also difference in study population and exclusion criteria [19,20].

Conclusion and Recommendations:
The results of the current study showed that the usage of prophylactic antibiotics before skin incision and its usage at cord clamping are equally effective in preventing postoperative infective complications.

References

