

# Comparing the effectiveness of broad spectrum antibiotic prophylaxis with single agent antibiotic prophylaxis to prevent post-cesarean section infection

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## Original Article

### Abstract

**Introduction:** The rate of cesarean delivery is increasing. Infection is one of the most frequent and important complications of emergency cesarean section. Infection prophylaxis has an important role to reduce post-cesarean delivery complication. The aim of this study was to compare the effectiveness of broad spectrum antibiotic prophylaxis (Azithromycin+Cephalotin) with single agent antibiotic prophylaxis (Cephalotin) to prevent post-cesarean section infection in Shariati hospital patient since August 2012 to August 2013.

**Methods:** This clinical trial study was carried out in Shariati hospital of Bandar Abbas, Iran. 424 pregnant women were recruited and divided to two groups. Group 1 received Azithromycin and Cephalotin as a preoperative antibiotic prophylaxis and group 2 receives routine antibiotic regime (Cephalotin and placebo). To find any signs or symptoms of post-cesarean infection, patients were visited one month after discharge. Collected data entered to SPSS software version 16 and descriptive and comparative test were performed.

**Results:** Our findings show that during one month after cesarian, in 4.3% (10 cases) of group 1 patients and 25.5% (55 cases) of group 2 patients, symptoms and signs of infection were observed. The difference between two groups was significant (P=0.000). We found no significant difference between demographic and other medical details.

**Conclusion:** Azithromycin have a significant effect on prevention of post-cesarean infection. Increasing the use of this broad spectrum agent as a part of antibiotic prophylaxis can decrease wound infection and other infectious complications of cesarean delivery.

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### Introduction:

Cesarean Delivery (CD) is one of the most common surgeries that is performed in the United States. Because of the high rate of CD, estimation of post-cesarean infection is so important. Normal rate of this kind of infection ranges from 7% to

20% depending on obstetric and demographic variables (1). Some while after cesarean delivery, maternal complications may result from a number of infections such as surgical site infection (SSI), endometritis and urinary tract infection (2). For the most patients, SSIs are not life threatening, but they

have considerable effect on the length of hospital stay and social implications for the parents and the newborn. In spite of that, in low income countries, infection remains among the top five causes of maternal mortality and SSI are a major cause of mortality and morbidity. CD is significantly associated with post-partum infections, and caused a 5 to 20 fold increase in risk of infection compared to vaginal delivery (3). The rate of infection following CD is reported about 1.1-25% as compared to 0.2-5.5% in vaginal delivery (4). Endometritis occur in 50% of pregnant women who had developed to post-cesarean section infection, but this can be diminish by 50% or even more with the use of prophylactic antibiotics. Geographical properties also can impact on the prevalence of postpartum UTI and wound infection (WI) (5). With or without endometritis, WI takes place in more than 10% of CD despite the suitable antibiotic prophylaxis administered, and also is 50% higher in emergency compared with elective CD. Infection during 30 days after cesarean section occurs in 7.6% of women following CD compared to 1.6% following vaginal delivery (6).

Incidence of post-cesarean infectious complications can be preventable by prophylactic antibiotics by as much as 75% in emergency and elective cesarean sections. First generation cephalosporins antibiotics are the most commonly used agents (2). Prophylactic antibiotics reduce the chance of SSI incidence and evidence-based guidelines recommend use of antibiotics prior to incision. Benefits of metronidazole, cephazolin, and tinidazole were evident in recent studies. The common causative organisms are *Ureaplasmas*, *Mycoplasmas*, anaerobes, *vaginalis* and these organisms are also sometimes isolated from amniotic fluid and the chorion at the time of CD (7).

The use of first generation cephalosporins such as cefazolin and cephalotin provides antibiotic activity against *Mycoplasmas* and *Ureaplasmas* but may cause the resistant organisms like anaerobes. Thus there is an attempt to extend antibiotic coverage by adding broad spectrum antibiotics to first generation cephalosporins.

Broad-spectrum antibiotics are associated with a significant reduction in infection rates, WI and endometritis. Broad-spectrum antibiotics also reduce the length of hospital stay (3). An appropriate

option as a second line agent for prophylaxis is azithromycin, which has a long half-life and some benefits such as high tissue concentrations, and low transplacental passage. In addition, azithromycin is active against *Ureaplasmas* as well as aerobes and anaerobes. These properties make this agent a stronger preventer against endometritis and WI than first generation cephalosporins. Using azithromycin as a part of prophylaxis also may prevent neonatal chronic lung disease and sepsis (8).

Although some studies favor single-agent preoperative antibiotics prophylaxis (6,9,10), but recent data suggest that the addition of azithromycin to the standard narrow-spectrum single-agent cephalosporin prophylaxis reduced the rates of endometritis and surgical wound infections after cesarean delivery (11). So in this study we decided to compare the effectiveness of broad spectrum antibiotic prophylaxis (Azithromycin + Cephalotin) with single agent antibiotic prophylaxis (Cephalotin) to prevent of post C/S infection in "Dr. Shariati Hospital" patient since August 2011 till August 2012.

## Methods:

In this randomized clinical trial study that was performed in Shariati gynecology and obstetrics hospital in Bandar Abbas, 424 pregnant women were recruited from August 2012 to August 2013.

Convenience sampling carried out to select patients. Research protocol was approved by the Human

Research Ethics Committee of Bandar Abbas medical science university. Eligible Women to participate in this study were who was above 14 years old with gestational age more than 24 weeks and scheduled to have an emergency cesarean section. Other criteria were spontaneously labor or induced labor (active labor, at least 3-4cm dilatation with uterus contraction), rupture of membranes within 4 hour prior the termination, meconium passage before section and non-cephalic presentation with uterus contraction. A checklist was used to record patient's demographic, medical and obstetric details. After collecting basic information about patients, inappropriate participants were excluded from study.

Exclusion criteria were multiple Pregnancy, Diabetes, allergic reaction toward Azitromycine, vaginal delivery, elective cesarean section before labor time or rupture of membranes, patients who have contraindication to receive antibiotics such as fetal distress of umbilical cord prolapsed, history of Azitromycine or Erythromicine use in one last week, clinical finding about corioamnionitis, intra uterin fetal death or severe fetal anomalies, pulmonary edema or chronic heart failure (EF < 45%), immunosupretion, HIV infection (CD4 < 200), active liver diseases, significant renal disease, patients who are under hemodialysis or have Cr > 2, preeclampsia and patients who have no prenatal care. Patients randomly divided to two groups. We used computer-generated randomization to prevent human bias in randomization. Before starting the study, trial project described to patients and a written consent took from all patients.

In the group 1, a single doses of intravenous Cephalotin (2gr) and Azitromycine (1gr) versus a single preoperative dose of intravenous Cephalotin (2gr) preoperative in group 2 were administered. All the patients were hospitalized at least for 48 hours after cesarean section. During first 48 hours after cesarean section, patients in both groups were visited to check out about any sign or symptoms about fever, wound infection and endometritis, twice a day by a particular gynecologist for each group. Some routine information about symptoms of fever, wound infection and endometritis were gave to the patients before discharge and asked them to back to the hospital if they develop to these symptoms. Patients were visited again 1 month after discharge to evaluate the presence of any kind of infections. Patients information in hospitalization period and 1 month after discharge, gathered and entered to SPSS statistics software. Categorical data were presented as frequency (percentage), and continuous data were reported as mean standard deviation. Categorical variables were compared using Chi-squared test. All P-values were two-tailed and a  $P < 0.05$  was considered to indicate significance.

## Results:

In total, 424 pregnant women were evaluated after cesarean section. Group 1 contains 216 (49.1%) and group 2 contains 208 (50.9%) participants. Mean age in group 1 was 26.03 years old and in group 2 was years 25.73 old. We found no significant statistical differences between mean age of two groups ( $P > 0.05$ ). As we mentioned before, one of the inclusion criteria was emergency cesarean sections. Table number 1 depicts the causes of emergency cesarean section indications as subgroups in each group. There is no significant difference between two groups in cesarean section indications ( $P > 0.05$ ).

Statistics analyses show that there is no deference in demographic, medical and obstetric status between two groups.

Morbidity of post-cesarean section Infection evaluated 1 month after discharge. Totally 359 (84.7%) patients from have no sign or symptoms of infection, and 65 patients developed to pos-cesarean complications. Sing and symptoms of infection found in 10 patient of group 1 and in 55 patients of group 2. The statistics difference between infection frequency in group 1 and 2 were strongly significant (0.000). Details of post-cesarean infection in both groups are showed in figure 1.

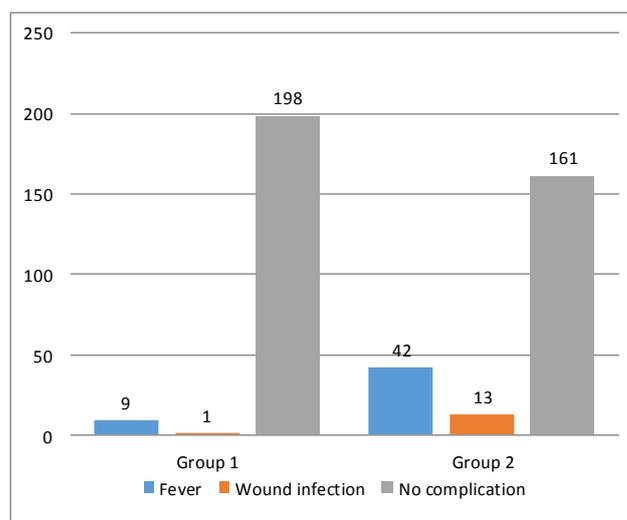


Figure 1. Details of post-cesarean infection

**Table 1. Indications of cesarean section**

	Repeat	TM <sup>1</sup>	Fm <sup>2</sup>	OCT <sup>3</sup>	FHR <sup>4</sup>	Abruption	Induction	Oligohydram	FP <sup>5</sup>	Breech	Apr <sup>6</sup>	Prom <sup>7</sup>	Macrosomia
<b>Group 1</b>	81 (38.9)	55 (26.4)	3 (1.4)	11 (5.3)	23 (11.1)	2 (1)	7 (3.4)	3 (1.4)	8 (3.8)	12 (5.8)	1 (0.5)	1 (0.5)	0 (0)
<b>Group 2</b>	58 (27.5)	62 (29.4)	2 (0.9)	14 (6.6)	26 (12.3)	0 (0)	3 (1.4)	7 (3.3)	9 (4.3)	23 (10.9)	1 (0.5)	0 (0)	1 (0.5)
<b>Total</b>	139 (33.2)	117 (27.9)	5 (1.2)	25 (6)	49 (11.7)	2 (0.5)	10 (2.4)	139 (33.2)	17 (4.1)	35 (8.4)	2 (0.5)	1 (0.2)	1 (0.2)

1-TM: Tick meconium 2- FM: Fetal movement 3- OCT: Oxytocin challenge test 4- FHR: Fetal Heart Rate 5- FP: Failure progress 6- APR: Anterior and posterior repair 7- PROM: premature rupture of membrane

### Conclusion:

Post-cesarean section infectious complications are commonly occurred that causes considerable morbidity (endometritis and wound infection) and longer hospital stay (1). These complications are rarely life threatening but in a few cases can cause necrotizing fasciitis. The rate of post-cesarean infections is higher than in comparable other surgical procedures. Many studies have been proven the role of antibiotic prophylaxis in reducing the incidence of post-cesarean infection (12).

Suggested plan to administer antibiotic prophylaxis for all kind of surgery includes cesarean section is administration of the drug just before skin incision. Other studies showed that the 30-65% reduction in wound infection rate and 60-70% reduction in endometritis rate after antibiotic prophylaxis (9,13). In our study, the rate of post-cesarean section morbidity in all participants was considerably high (about 15.3%) while in other studies, the infection rate is not higher than 3% when antibiotics are given prior to skin incision. In the study of Brown and colleagues, Cephalotin was administered as a preoperative prophylactic antibiotic. In this study, the rate of infection was more than 3% (6). Group based results in our study show that 10 (4.8%) patients who received Azithromycin and Cephalotin have signs of infection and 55 (25.5%) patients, who received Cephalotin alone, were developed to post-cesarean section infections. Difference between two groups are statistically significant ( $P=0.000$ ) and prove that the effective role of Azithromycin on bacterial infection prevention. Although we found significant differences between case and control groups, but analysis based on cesarean section causes showed that broad spectrum antibiotic (Azithromycin) is

effective only in patients with thick meconium diagnosis. In other cases, there was no significant difference between case and control groups. Maybe this controversy between tick meconium subgroup and others is because of small number of participants in rest of cesarean section subgroups.

Cephalotin is a member of first generation cephalosporins that provides antibiotic activity against Mycoplasma and Ureaplasma but after chronic use, it may cause an increase the resistance in organisms. There is some recommendation to add agents such as Azithromycin to extend the cover (14). Some clinical trials compared the prophylaxis effect of narrow spectrum antibiotics such as first generation cephalosporins with wide spectrum antibiotics like Azithromycin or gentamycin. Broad spectrum antibiotics were associated with a statistically significant reduction in infection rate. Azithromycin have a long half-life (68 hours), low transplacental passage and high tissue concentration. Also Azithromycin is active against aerobic and anaerobic bacteria such as ureaplasmas. This antibiotic may prevent neonatal chronic lung disease and neonatal sepsis (8) so we would suggest the routine administration of Azithromycin as a part of preoperative cesarean section antibiotic prophylaxis.

On the basis of our findings, adding Azithromycin to the routine antibiotic prophylaxis regime (Cephalotin alone) rather than Cephalotin alone, is significantly more effective to reduce the post-cesarean section infections.

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## مقایسه اثربخشی پروبیلاکسی آنتی بیوتیکی وسیع الطیف با آزیترومایسین به همراه کفلین نسبت به کفلین تنها، در جلوگیری از تب و عفونت بعد از سزارین اورژانسی

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### چکیده

**مقدمه:** آمار زایمان به روش سزارین در حال افزایش است. عفونت یکی از مهمترین و تکرار شونده ترین عارضه سزارین اورژانسی می باشد. پروبیلاکسی عفونت مهمترین نقش را در کاهش این عارضه بعد از سزارین دارد. هدف از این مطالعه، مقایسه آنتی بیوتیک وسیع الطیف (آزیترومایسین + سفالوتین) با یک آنتی بیوتیک تنها (سفالوتین) در پیشگیری از این عفونت بعد از سزارین اورژانسی در بیماران مراجعه کننده به بیمارستان دکتر شریعتی بندرعباس از مردادماه ۱۳۹۰ لغایت مردادماه ۱۳۹۱ می باشد.

**روش کار:** در این مطالعه کارآزمایی بالینی، ۴۲۴ نفر خانم باردار مراجعه کننده به دو دسته تقسیم شدند: گروه اول، آزیترومایسین به علاوه سفالوتین به عنوان پروبیلاکسی قبل از عمل دریافت کردند و گروه دوم، سفالوتین به علاوه پلاسبو. جهت پیدا کردن هر علامت یا نشانه ای از عفونت بعد از عمل، بیماران تا یک ماه پس از عمل تحت پیگیری بودند. یافته ها وارد سیستم SPSS 16 شدند و مقایسه انجام شد.

**نتایج:** یافته های ما نشان داد که ۱۰٪ (۴/۸ درصد) بیمار از گروه اول و ۵۵٪ (۲۵/۵ درصد) بیمار از گروه دوم مبتلا به علامت یا نشانه ای از عفونت شدند. در طی یک ماه پس از عمل، اختلاف بین دو گروه ( $P=0/000$ ) از نظر آماری معنی دار بود.

**نتیجه گیری:** آزیترومایسین به طور چشمگیری از عفونت بعد از عمل جلوگیری کرد. استفاده از آنتی بیوتیک وسیع الطیف عفونت و عوارض عفونی بعد از سزارین را کاهش می دهد و توصیه می گردد.

**کلیدواژه ها:** آنتی بیوتیک، عفونت، سزارین

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