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**RESEARCH**

## The Effect of Giving Prophylactic Antibiotic Ceftriaxone and Cefazolin and Giving Ceftriaxone Before and After Surgery to The Risk of Postoperative Wound Infection in Postoperative Patients

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**Abstract**

**Objective :** To determine the effect of giving prophylactic antibiotic ceftriaxone and cefazolin and giving ceftriaxone before and after surgery to the risk of postoperative wound infection in postoperative patients.

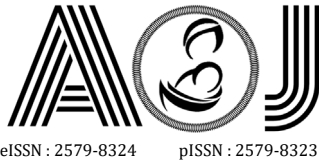
**Method:** This study was an experimental study with a post test control group design that looked at the differences in the effect of administration of ceftriaxone, cefazolin, and ceftriaxone before and after surgery on the risk of postoperative wound infection. The population in this study were patients planned for surgery in the Obstetric and Gynecologic Department of Dr. M. Djamil General Hospital, Padang. The number of samples used by 30 people with a group of 10 people each group. The study began in August until the number of samples was fulfilled. Univariate analysis was used to see the frequency, percentage, mean, and standard deviation. Bivariate analysis using Chi-square test with 95% CI ( $\alpha < 0.05$ ) was used to see differences in the effect of the three antibiotic procedures.

**Results:** There were no cases of postoperative wound infection based on the three procedures used. There was no difference in the effect of prophylactic antibiotics in postoperative infections. **Conclusion:** There was no difference in the effect of the three procedures for prophylactic antibiotics in postoperative infections.

**Keywords:** Prophylactic Antibiotics, Surgical Wound Infections, Cefazolin, Ceftriaxone, Superficial incisional SSI

**INTRODUCTION**

Nosocomial infections are infections in patients who get germs from the hospital. Its prevalence in the world is still unknown due to data collection difficulties. WHO estimates that out of 100 patients treated in hospital, 7 patients in developed countries and 15 patients in developing countries have nosocomial infections. The endemic to nosocomial infections is 2–3 times higher in developing countries, leading to increased morbidity, mortality, and medical costs. One of the most common nosocomial infections is postoperative infection.<sup>1</sup>



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In a preliminary study conducted by researchers regarding the pattern of bacteria and their sensitivity to antibiotics in patients treated in the Inpatient Room, the Department of Obstetrics and Gynecology, Dr. M. Djamil Padang, found that the most contributor to infection rates was postoperative infections.<sup>1,2</sup>

Postoperative infection is the most preventable nosocomial infection. However, this infection remains an important cause of postoperative morbidity, prolonged care, and death. Postoperative infection mortality rate reaches 3% and is a nosocomial infection that absorbs the highest cost of care. Therefore, the prevention of postoperative infection receives special attention from experts. Some investigators concluded that the incidence of postoperative infection reflects the quality of hospital care.

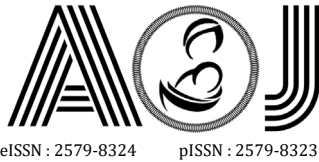
Postoperative infection is multifactorial. Prevention requires integrated checks before, during and after surgery.<sup>1</sup> Various efforts have been made, such as increasing operating room ventilation, sterilization, barriers, surgical techniques, and prophylactic antibiotics.

Many studies have studied the effectiveness of prophylactic antibiotics in reducing morbidity due to postoperative infections and have largely supported their use.<sup>4</sup> Experts also recommend the use of prophylactic antibiotics in obstetrics and gynecology in several types of procedures. A meta-analysis of 17 studies in 2,752 patients showed that prophylactic antibiotics reduced infection rates by 65% in patients undergoing hysterectomy. American College of Obstetricians and Gynecologist (ACOG) recommends the use of prophylactic antibiotics in hysterectomy, urogynecological procedures, hysterosalpingograms, induced abortions, and does not recommend them for operations with low risk of infection such as laparoscopy, tubal sterilization, and hysteroscopy.<sup>5</sup>

Antibiotics that were effective against gram-positive, gram-negative, and anaerobic bacteria were selected as prophylaxis in cesarean delivery. A wide variety of antibiotics have been tested. A retrospective study of 2,280 non-selective caesarean section reported that cefazoline and cefotaxime were effective in preventing post-cesarean endometritis. Similar to that study, a meta-analysis of 27 studies confirmed that beta-lactams and cephalosporins were effective prophylaxis.<sup>6</sup>

Cephazolin is a first generation cephalosporin that is sensitive to gram-positive and some gram-negative bacteria such as *E. Coli*, *Proteus*, and *Klabsiella*. Cephazolin has been widely recommended as a prophylactic antibiotic in surgical procedures. Cephazolin has the advantage of having a moderate half-life of around 120 minutes, providing protection during surgery that ranges from one to two hours. Excellent anti-staphylococcal activity compared to ceftriaxone because it is more sensitive to the staphylococcal group. In addition, the incidence of allergic reactions is lower than ceftriaxone. However, if the duration of the operation is more than 2-3 hours, then a second dose is required.<sup>7,8</sup>

Ceftriaxone is a second generation cephalosporin which has a broader spectrum than



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cefazolin. Apart from being effective against gram-positive, ceftriaxone is more sensitive to gram-negative than cefazolin and anaerobic bacteria.<sup>7</sup>

There are variations in the use of prophylactic antibiotics in various hospitals in general as well as at the Central General Hospital Dr. M. Djamil himself, the use of prophylactic antibiotics still uses ceftriaxone in most of the inpatient installations, especially the Obstetrics and Gynecology Section. Where this is different from the recommendations prophylactic antibiotics issued by ACOG, WHO, RSUP M Djamil and POGI which recommend giving cefazolin that is a cephalosporins generation First, based on this explanation, the researchers were interested in observing the differences in the effectiveness of the prophylactic antibiotics of ceftriaxone and cefazolin and the antibiotics ceftriaxone given before and after surgery in elective cesarean section patients in the Inpatient Room of the Obstetrics and Gynecology Department, Dr. M. Djamil Padang.

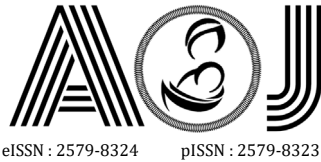
## METHOD

This research is an experimental study with post test control group design. The research was conducted from August 2019 until the number of samples was met. The research was conducted in the Inpatient Department of Obstetrics and Gynecology, RSUPDr. M. Djamil, Padang. The population in this study were patients who planned to perform clean and clean contaminated surgery at the Midwifery Department of Dr. M. Djamil Padang who met the inclusion and exclusion criteria. Sampling in this study using the method consecutive sampling. Every patient planned for surgery at the Obstetrics and Gynecology Department Dr. M. Djamil Padang who met the inclusion and exclusion criteria will be sampled. Each sample will get information about the research including the purpose of the research, how the research was carried out, benefits, rights and obligations, and risks as a sample. Samples will be signed informed consent as a sign of approval used as research samples. Data analysis was performed with a computer program. The assessment was carried out in 3 groups, namely the group that received cefazoline antibiotics and the group that received ceftriaxone antibiotics and the group that received 2 grams of ceftriaxone antibiotics before surgery plus 2x1 grams for three postoperative days. The data of each group was tested using the test Chi Square, if the value of  $E < 5$  is found, then the statistical test to be performed is Kruskal Wallis.

## RESULTS

### Normality test

Normality test is performed using the Shapiro Wilk test to determine whether the data is normally distributed or not. The results of the data normality test show that age and BMI are normally distributed ( $p \geq 0.05$ ), and can be seen in Table 1 below:



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**Table 1.** Data normality test

Variable	N	Mean ± SD	p-value
Age	30	34,10 ± 6,89	0,09
BMI	30	22,83 ± 2,78	0,05

**Table 2.** Characteristics of Respondents by Age and BMI

Characteristics	Mean ± SD
Age	34,10 ± 6,89
BMI	22,83 ± 2,78

Based on Table 2, it is known that the mean age of the respondents was  $34.10 \pm 6.89$  years and BMI  $22.83 \pm 2.78$ .

**Table 3.** Case group research sample

Case Group	f (%)
- Obstetrics cases	26 (86,7%)
- Gynecological cases	4 (13,3%)

Based on Table 3 it is known that as many as 26 respondents (86.7%) had obstetric cases and 4 respondents (13.3%) had gynecological cases.

**Table 4.** Effects of ceftriaxone administration

Variabel	N	Infektion	No infection
Administration of ceftriaxone	10	0 (0%)	10 (100%)

Based on Table 4, it is known that all respondents (100%) who were given ceftriaxone antibiotics did not experience infection.

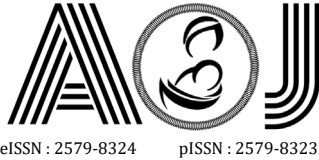
**Table 5.** Effects of cephalosporin administration

Variabel	N	Infektion	No infection
Administration of cephalosporin	10	0 (0%)	10 (100%)

Based on Table 5, it is known that all respondents (100%) who were given cefazolin antibiotics did not experience infection.

**Table 6.** Effect of ceftriaxone administration before and after operation

Variabel	N	Infektion	No infection
Administration of ceftriaxone before and after operation	10	0 (0%)	10 (100%)



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Based on Table 6, it is known that all respondents (100%) who were given ceftriaxone antibiotics before and after surgery did not experience infection.

**Table 7.** Differences in the Effect of Antibiotics

Variabel	N	Infektion	No infection
Administration of ceftriaxone	10	0 (0%)	10 (100%)
Administration of cephalosporin	10	0 (0%)	10 (100%)
Administration of ceftriaxone before and after operation	10	0 (0%)	10 (100%)

Based on Table 7, it is known that all respondents who were given prophylactic antibiotics cefazoline and ceftriaxone and ceftriaxone antibiotics before and after surgery did not experience infection.

Statistical tests could not be performed because there was no incidence of infection in each sample group.

## DISCUSSION

Based on the results of this study, it is known that the mean age of the respondents was  $34.10 \pm 6.89$  years. The mean BMI of respondents was in the normal category, namely  $22.83 \pm 2.78$ . More than half of the respondents (86.7%) in this study were obstetric cases.

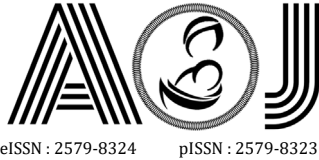
Research in the UK shows that overweight and obesity is associated with an increased risk of postoperative infection. This study accommodated 206 hospitals and observed 350,089 surgeries from 1 January 2007 to 31 December

2011, in which 4,832 were known to have had postoperative infections. In this study, 42.33% were classified as obese, 37.51% overweight, 19.47% normoweight, and 0.69% underweight.

This study concluded that obesity is strongly associated with the risk of postoperative infection in various types of surgery. The risk of postoperative infection in abdominal hysterectomy is linearly associated with an increase in BMI.<sup>9</sup>

Obese patients show decreased subcutaneous tissue oxygenation and require a larger oxygen fraction to achieve the same arterial oxygen pressure as normoweight patients. Oxygen insufficiency causes slow wound healing process and inhibits the work of immune cells in preventing the development of bacteria. Due to poor tissue oxygenation, an adequate prophylactic antibiotic concentration is required so that the prophylactic antibiotic dosage of obese patients must be differentiated.<sup>9</sup>

Age is a risk factor for postoperative wound infection. Antonella's research, et al (2015) shows the incidence of postoperative infections by age  $\geq 65$  years and  $<65$  years were 6.2 and 2.2 per 100 surgical procedures, but this figure was not significant. NHS stipulates infection



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risk index ( IRI) based on ASA status, duration of surgery, and class of surgical wound. The incidence of postoperative infection in patients with IRI 0, 1, and 3 were 1; 9.7; and 30 per 100 operations. The age factor is independent in causing postoperative infection and affects the ASA score with a threshold of 65 years. In addition, it was found that most of the patients who reported having IRI of more than 1 or 2 were elderly patients. <sup>10</sup>

In this study, it was found that the case group was more in cesarean section, namely 86.7% while gynecological surgery 13.3%. In line with these numbers, National Hospital Discharge Survey ( NHDS) shows that of the 36.3 million obstetric and gynecological surgeries performed in the United States from 1979 to 2006, 64% were cesarean sections, 29% were gynecological operations, and 7% were combined obstetric and gynecological operations. <sup>3</sup>. While research at Ulin Hospital, Banjarmasin showed that the proportion of caesarean section was 64.7% and gynecological operations were as much 35.3%. <sup>11</sup>

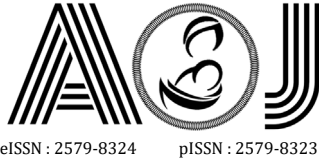
The results of this study indicate that none of the patients given ceftriaxone antibiotics had postoperative infections. A prospective cohort study conducted in Thailand showed no difference in the incidence of postoperative infection between patients receiving ceftriaxone and ampicillin. <sup>12</sup>

Previous studies have shown ceftriaxone administration is able to prevent the incidence of postoperative infection, however, as more and more use of this antibiotic in daily practice. The incidence of resistance is increasing and the result is a decrease in its effectiveness as an infection-preventing agent, and will also increase the global problem where antibiotic resistance is increasing. <sup>13</sup>

Ceftriaxone is a second generation cephalosporin that has a broad spectrum. Ceftriaxone is more sensitive to gram-negative than cefazolin and anaerobic bacteria. <sup>7</sup> Ceftriaxone has a wider spectrum against gram-negative bacteria such as Haemophilus influenzae, Moraxella catarrhalis, Escherichia coli, Klabsiella pneumonia, Neisseria sp, and Enterobacter sp, Serratia mercescens, and Acinetobacter sp. However, these bacteria are rarely found in surgical wound swabs <sup>8,14,15</sup>

Research conducted by Chiu et al (2007) shows that resistance rates Streptococcus pneumoniae to ceftriaxone significantly increased in Taiwan in 2005. About 90% of the isolates resistant to ceftriaxone were found in 4 serotypes. There was a change in the 7 amino acids PBP which contributed to the resistance of these bacteria to ceftriaxone. <sup>16</sup>

Research conducted at Basancon Hospital shows that there is an increasing use of the antibiotic ceftriaxone. At the same time, this study found an increase in isolates E. cloacae that is resistant to ceftriaxone. This study concluded that there is a specific correlation between ceftriaxone use and resistance in clinical isolates E. cloacae. <sup>17</sup>



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The results of this study indicate that no patient given a single dose of cefazoline antibiotics experienced postoperative infections. Cephazolin 2 gram IV as a single dose is given 30-60 minutes preoperatively. <sup>6,13,18</sup>

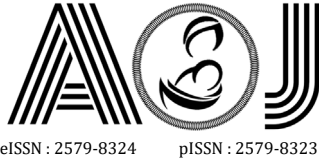
Cephazolin is a member of Cephalosporin Generation I. Cefazolin is active against gram-positive and some gram-negative bacteria such as E. Coli, Proteus, and Klabsiella. <sup>7</sup> Cephazolin has been widely recommended as a prophylactic antibiotic in surgical procedures. Cephazolin has the advantages of: 1) its moderate half-life, which is about 120 minutes, so it is considered sufficient to provide protection during surgery with a duration of 1-2 hours; 2) excellent anti-staphylococcal activity; 3) and the incidence of allergic reactions is lower than ceftriaxone.

From the results of this study, it is known that of the three procedures for giving antibiotics, namely ceftriaxone antibiotics before surgery, cefazoline antibiotics before surgery, and ceftriaxone antibiotics before and after surgery, no patient (0%) experienced postoperative infections. Yulia's research results et al ( 2018) at the Pasuruan Regency Regional Hospital, it is known that out of 100 people who were given antibiotics before surgery, two of them experienced surgical wound infections (ILO). These patients were given different types of antibiotics, namely ampicillin, cefuroxime, ceftriaxone, cefazolin, metronidazole, and gentamicin. However, the investigators did not mention the type of antibiotics given to patients with ILO. <sup>19</sup>

The use of antibiotics in RSUP DR M Djamil is still varied in several parts or departments, for the use of prophylactic antibiotics in the obstetrics section 2 grams of ceftriaxone antibiotics are used before surgery, some cases are given 2x1g ceftriaxone antibiotics after surgery, and some are not given antibiotics after surgery. Currently, the prophylactic antibiotic cephazolin 2gr 30 minutes before surgery is also used, according to the procedure from PPRA RSUP DR M Djamil. Meanwhile, the surgical department still used the prophylactic antibiotic ceftriaxone followed by the administration of ceftriaxone after surgery, as well as the ENT department. <sup>18,20</sup>

Guideline published by American College of Obstetricians and Gynecologist recommends administering a single dose of 2 gram intravenous cefazoline as prophylaxis before cesarean section, as well as for other gynecological surgeries <sup>10</sup>.

This recommendation is in line with the guidelines for the use of antibiotics published by Dr. M. Djamil Padang in 2018 and the Indonesian Association of Gynecological Obstetrics (POGI) in 2013. <sup>6,18</sup>



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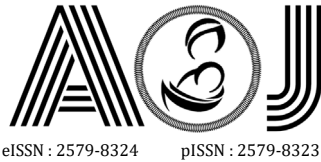
**Table 8.** Comparison of Ceftriaxone and Cephazoline as Prophylaxis

Procedure	Deficiency	Advantages
Cephazoline 2 gram single dose	<ul style="list-style-type: none"> <li>- Requires additional doses if the duration of operation is &gt; 3 hours</li> <li>- Unit price is more expensive</li> <li>- The spectrum is narrower</li> </ul>	<ul style="list-style-type: none"> <li>- Sensitive to staphylococci</li> <li>- A single dose is considered effective in preventing postoperative infections</li> <li>- The half-life of the drug is sufficient to protect against the duration of surgery</li> <li>- Lower drug toxicity</li> <li>- Few side effects</li> <li>- The total cost is cheaper than multiple doses of ceftriaxone</li> <li>- Low risk of resistance</li> <li>- In accordance with the recommendations of ACOG, POGI, RSUP M Djamil</li> </ul>
Ceftriaxone 2 gram single dose	<ul style="list-style-type: none"> <li>- Less sensitive than cefazolin to staphylococci</li> <li>- Higher toxicity</li> <li>- Side effects are more common</li> <li>- Considered less effective if given a single dose because of the pattern of germs and bacterial resistance due to extensive use of ceftriaxone in hospitals</li> <li>- Not in accordance with the recommendations of ACOG, POGI, RSUP M Djamil</li> </ul>	<ul style="list-style-type: none"> <li>- Broad spectrum compared to cefazolin</li> <li>- The unit price is cheaper</li> </ul>
Ceftriaxone before and after operation	<ul style="list-style-type: none"> <li>- High total cost</li> <li>- Higher toxicity</li> <li>- Side effects are more common</li> <li>- High risk of resistance</li> <li>- Not in accordance with the recommendations of ACOG, POGI, RSUP M Djamil</li> </ul>	<ul style="list-style-type: none"> <li>- Rated effective in preventing postoperative infections</li> </ul>

**CONCLUSION**

There is an effect of giving ceftriaxone and cefazoline antibiotics in preventing postoperative infections. There is an effect of giving ceftriaxone antibiotics before and after surgery in preventing postoperative infections. However, there was no difference in the effect of prophylactic antibiotics cefazolin and ceftriaxone and ceftriaxone antibiotics before and after surgery in preventing postoperative infections.





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