THE EFFECTIVENESS OF THE USE OF ANTIBIOTICS PROPHYLAXIS IN PREVENTION OF SURGICAL SITE INFECTION IN CAESAREAN SECTION

A Scoping Review

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ABSTRACT

Background: Caesarean section is still a type of surgical procedure most general work done throughout the world, including in the State of Indonesia with a trend of the percentage between 30-80%. Sectio caesarean delivery is often associated with wound complications such as wound infection, hematoma / seroma, wound dehiscence, and endometritis with an increased risk of five to ten times, especially complications related to infection. Post-caesarean section wound complications occur in 2-16% of women and are a significant cause of maternal morbidity and mortality.

Purpose: This systematic literature review aims to analyze the effectiveness of prophylactic antibiotics in preventing infection of the surgical site in patients undergoing cesarean section.

Methods: The literature search was carried out by involving three online databases, namely PubMed, ProQuest, and Scopus which were published between 2016 - 2020 with the main keyword used is prophylaxis antibiotic; surgical site infection; and sectio caesarea.

Results: There were 11 articles selected from the literature search process. Based on the results of the review of the article, the entire literature found states that the use of prophylactic antibiotics is effective in preventing the incidence of infection in the surgical area after cesarean section. Its effectiveness is increased by giving combination antibiotics compared to administration of single antibiotics. Most of the prophylactic antibiotics used in selected studies were cephalosporin antibiotics.

Conclusion: Based on a systematic review of the literature that has been carried out, it can be concluded that prophylactic antibiotics before the procedure caesarean section can reduce the incidence of postoperative infection.

Keywords: Antibiotic Prophylaxis, Surgical Site Infection, Caesarean Section

1. INTRODUCTION

Caesarean section or sectio caesarea is still the most common type of surgical procedure performed worldwide (La Rosa et al., 2020). The incidence of sectio caesarea has increased from year to year worldwide, exceeding the WHO recommended range, which is 10-15% of all deliveries. In America, sectio caesarean delivery covers 32% of total deliveries (Kawakita, Huang and Landy, 2018). The delivery rate for sectio caesarea in Indonesia shows a stable trend with a percentage of between 30-80% of total deliveries (Hapsari and Hendraningsih, 2018). Based on national survey data by the Ministry of Health of the Republic of Indonesia in 2007 there were 927,000 sectio caesarean deliveries out of a total of 4,030,000 deliveries (Ferinawati and Hartati, 2019). National survey data in 2012 showed that there were 921,000 sectio caesarean deliveries out of a total of 4,039,000 deliveries in Indonesia (Hapsari and Hendraningsih, 2018). Based on the results of the 2018 Basic Health Research (Risksdas), the incidence of sectio caesarea in Indonesia is 17.6%, with the highest prevalence in DKI Jakarta, which is 31.3% and the lowest is in the Papua region of 6.7%.
Sectio caesarean delivery is often associated with wound complications such as wound infection, hematoma / seroma, wound dehiscence, and endometritis (Mackeen, Khalifeh, et al., 2014; Peleg et al., 2016). Compared with vaginal delivery, women who undergo caesarean section have a five to ten fold risk of complications related to infection (La Rosa et al., 2020). Post-caesarean section wound complications occur in 2-16% of women and are a significant cause of maternal morbidity and mortality. Complications of caesarean section are also the main cause of patients having a longer duration of stay in the hospital (Blumenfeld et al., 2015). Thus, wound complications in women who undergo caesarean section also become a burden on the health care system of a country (Olsen et al., 2010).

In the last few decades, the routine use of pre-operative antibiotics in women who are about to undergo cesarean section delivery is considered to be able to reduce the number of infection-related wound complications (American College of Obstetricians and Gynecologists, 2011). A systematic review recent Cochrane showed that postoperative complications of caesarean section delivery overall decreased by 60-70% in pregnant women who received preoperative prophylactic antibiotics (Smaill and Grivell, 2014). In addition, preoperative antibiotic administration did not show significant side effects in both the mother and the neonate (Mackeen, Packard, et al., 2014).

Given the high rate of cesarean section delivery and the high likelihood of infection-related wound complications in women undergoing sectio caesarea procedures in Indonesia and the potential use of prophylactic antibiotics in reducing the incidence of infection in surgical wounds, this literature review aims to examine the effectiveness of using prophylactic antibiotics in preventing surgical sites infection in patients undergoing cesarean section procedure.

II. METHODS

Data Sources

The method used in the writing of this scoping review is a systematic approach and selection process. Sources of literature were traced from national and international databases, namely PubMed, ProQuest, and Scopus. Additional searches were also carried out on government and non-government websites such as the Ministry of Health, Bureau of Statistics, and the World Health Organization (WHO).

Search library begins with developing specific keywords contained in the research questions such as prophylactic antibiotics, surgical site infection, and sectio caesarea. From these specific keywords, each synonym is searched to expand the search for literature. In each database, a search will be carried out based on the provisions of each database to obtain appropriate results. Search is not limited by geography, but will be limited to journals / articles in Indonesian and English. Samples to be taken are journals / articles published in the last 5 years (2016-2020).

Inclusion and Exclusion

Criteria The inclusion criteria for selected journals are using English or Indonesian, using human subjects, being journals for the last 5 years, and clinical studies using randomized controlled trials, cohort studies, and case controls. Meanwhile, the exclusion criteria for selected studies were systematic review, literature review, and complete access was not available.

III. RESULTS

The results of the study search and selection process are presented in Figure 1. A total of 800 potentially relevant studies were identified. Of these, 444 are duplicates. Of the remaining 356 studies, 324 were excluded after the title and abstract assessment. Of the remaining 32 records, only 11 studies had access available. Eligibility of 11 full-text articles was assessed, none were excluded. The methodological quality of the remaining 11 studies was assessed, of which 5 were randomized clinical trials, 4 were retrospective cohort studies, and 2 were prospective cohort studies.
Based on the results of the systematic search, it was found 11 literatures that met the inclusion criteria. Out of a total of 11 literature, 5 were randomized clinical trials, 4 were retrospective cohort studies, and 2 were prospective cohort studies. The study publication dates ranged from 2016 to 2020, and all were published in English. Data obtained from the United States consisted of 4 studies, while Indonesia, Israel, Germany, Thailand, China, India, and Kenya each obtained 1 study.

In general, the entire literature found states that the use of prophylactic antibiotics is effective in preventing the incidence of infection in the postoperative area after cesarean section.

A prospective cohort study involving 600 subjects, stated that the incidence of surgical site infection in patients receiving perioperative prophylactic antibiotics was lower (4.0%) than patients who only received postoperative prophylactic antibiotics (9.3%) (Sway et al., 2020).

A single blind randomized clinical trial involving 46 research subjects stated that there was no difference in the incidence of surgical site infections in pregnant women who received single dose cefazolin prophylactic antibiotics and those who received double doses of cefazolin (Purbadi and Fadli, 2017). These results are in line with a retrospective cohort study, which involved 730 study subjects, which stated that the incidence rate of surgical wound area infection after low dose cefazolin prophylactic antibiotics was 4%, while after high-dose cefazolin administration was 5% (La Rosa et al., 2020).

A retrospective cohort study involving a large sample (n = 6,584), compared the use of cephalosporin and non-cephalosporin prophylactic antibiotics and stated that the use of non-cephalosporin prophylactic antibiotics increased the odds ratio (OR 2.45; 95% CI 1.73–3.41) for regional infection. post-surgery cesarean section(Kawakita et al., 2018).

A retrospective cohort study involving 929 subjects, supports this finding by stating that the incidence rate of surgical site infection in women receiving beta-lactam antibiotics was 7%, while the non-beta-lactam group was 15% (p = 0.004 ) (Harris et al., 2019).
Assawapalanggool S et al, in their study which is a prospective observational cohort study, involving 4149 pregnant women who will undergo cesarean section, stated that the incidence of infection in the area of surgery after giving ceftriaxone prophylactic antibiotics with ampicillin, respectively 0.1% and 1.2%, but there was no difference in rate ratios statistically significant (RR, 1.10; 95% CI 0.58–2.08) between the two groups (Assawapalanggool et al., 2018).

Apart from the literature that mentions the effectiveness of standard prophylactic antibiotics in preventing the incidence of post-infection caesarean section, there is also a randomized clinical trial evaluating the effectiveness of adjuvant prophylactic antibiotics with azithromycin. The study, involving 1019 subjects, stated that administration of adjuvant prophylactic antibiotics with azithromycin after standard prophylactic antibiotics was significantly associated with a reduced risk of surgical site infection compared to the placebo group, with rates of incidence of infection in the surgical area of 2.4% and 6.6%, respectively (RR, 0.35; 95% CI, 0.22 to 0.56; P <0.001) (Tita et al., 2016). Another study by Jyothi et al, coincided with these findings by stating that patients receiving the combined prophylactic antibiotic cefazolin and azithromycin had a lower incidence of surgical site infections compared to the combination cefazolin and placebo group (p = 0.003) (Jyothi et al., 2019).

Another study by Valent et al, also examined the effectiveness of a combination of adjuvant prophylactic antibiotics postoperative cephalixin and oral metronidazole, which stated that the incidence of surgical site infections was lower in the cephalixin-metronidazole group (6.4%) than in the placebo group (15.4%), and found that the difference was statistically significant (difference, 9.0% [95% CI, 2.9% - 15.0%]; relative risk, 0.41 [95% CI, 0.22-0.77]; P = .01) (Valent et al., 2017).

One retrospective study also examined the association between the incidence of surgical site infection and timing of prophylactic antibiotics, between preoperative administration and shortly after cord clamping. Shoham et al, in their retrospective study involving 7339 research samples, stated that the incidence of surgical site infection in the group receiving preoperative prophylactic antibiotics was 2.32%, while in the prophylactic antibiotic immediately after cord clamping was 2.63% (Ben Shoham et al., 2019 ).

From a total of 11 literature that was found related to the effectiveness of antibiotic administration, there was one randomized clinical trial study involving 414 research subjects, by Hong et al., Stated that the incidence rate of infection in the surgical area in the group receiving prophylactic antibiotics and those not receiving prophylactic antibiotics was not different. which is statistically significant (x2 = 1.679, p = 0.195) (Hong et al., 2016).

IV. DISCUSSION

Selection of prophylactic antibiotics

There is debate about the benefits of prophylactic antibiotics for women undergoing elective cesarean section. A meta-analysis of 4 studies found that prophylactic antibiotics resulted in a reduction in postoperative fever (RR 0.25; 95% CI 0.14-0.44) and endometritis (RR 0.05; 95% CI 0.01-0.38) . Overall, these data support the recommendation to use prophylactic antibiotics for all women undergoing cesarean section.

Pregnant women who undergo delivery by cesarean section have a risk of complications from postoperative infections. The World Health Organization (WHO) also recommends routine prophylactic antibiotics for women undergoing elective and emergency cesarean sections. The standard recommended prophylactic antibiotic is the first generation cephalosporin or penicillin class, which is administered intravenously 15-60 minutes before skin incision (World Health Organization et al., 2015).

The American College of Obstetricians and Gynecologists (ACOG) recommends the use of antibiotics for all women undergoing cesarean section.1 Recommended antibiotics for use are first-generation cephalosporins as the antibiotic of choice unless significant drug allergy (anaphylaxis, angioedema, respiratory distress, or urticaria) is reported. . ACOG recommends the use of a clindamycin combination with an aminoglycoside class as a reasonable alternative for women with significant β-lactam allergies, although efficacy data comparing the use of standard alternative antibiotics with cefazolin are limited. Although there was no difference in the primary outcome, it was found that cellulitis was noted to be increased in relation to the use of standard alternative antibiotics compared to cefazolin. The increase in cellulitis could be explained by the effectiveness of cefazolin in controlling skin flora such as Streptococcus species and Staphylococcus species compared to non-β-lactam agents. (Chelmow, et al. 2001)
The choice of antibiotics is often based on the risk of wound infection according to the wound classification, the distribution of the normal flora of the area to be operated on and the pattern of antibiotic resistance in the hospital setting. Generally, broad spectrum antibiotics are preferred over narrow spectrum antibiotics and usually use cephalosporins. Cefazolin is generally recommended for gastroenterological, genito-urinary, and hepatobiliary operations (Bratzler et al., 2013).

The most studied antibiotics for surgical prophylaxis are cephalosporins. Cefazolin is a first-generation cephalosporin which is a pregnancy category B drug. When administered intravenously, its half-life is 1.8 hours. This provides good coverage for gram positive bacteria and moderate coverage for gram negative bacteria. In 1999 guidelines, the Centers for Disease Control and Prevention (CDC) recommends the use of prophylactic antibiotics in cesarean section. 1 to 2 grams intravenously and no later than 30 minutes before incision is recommended. Additional doses may be considered if the patient has more than 1500 L of blood loss or at 4 hours if the procedure lasts more than 4 hours. (Andrews, et al. 2003)

From this literature review, it is stated that the effectiveness of prophylactic antibiotics in preventing the incidence of surgical wound area infection is related to the class of antibiotics used. There are several antibiotic options that can be given before cesarean section. A study in the United States stated 95.5% of carriers used first-generation cephalosporin antibiotics; 84.4% used cefazolin (first generation cephalosporin) with bactericidal activity as a prophylactic for SC surgery. Its mechanism of action involves binding of penicillin-binding proteins to the inner cell wall, blocking cell wall synthesis, and ultimately leading to bacterial cell lysis. The use of cefazolin has been widely accepted based on its broad spectrum activity (gram positive, group B streptococci and gram negative) and at a relatively affordable cost (La Rosa et al., 2020).

From a study by Kawakita et al, it was found that the administration of beta-lactam antibiotics was more effective in preventing the incidence of post-surgery area infections cesarean compared to other antibiotics. In that study, 2.2% of women did not receive the prophylactic antibiotics recommended by the ACOG. The majority of those who received inappropriate alternative antibiotics received only one agent, clindamycin or gentamicin. Based on these data, we found a higher risk of wound complications with the use of clindamycin or gentamicin alone compared with the use of cefazolin. Therefore, using cefazolin for women with a history of beta-lactam allergy that is not significant can reduce the complication rate of post-caesarean wounds (Kawakita et al., 2018).

One study, by Harris et al, said in their study, patients who received non-β-lactam antibiotics were more likely to have wound complications, including infection, compared to those who received β-lactam antibiotics (14.6% vs. 6.7% ; p < 0.02). Gram-positive bacteria are the most common organisms isolated from cesarean section infection, so the bactericidal properties of cefazolin may help explain the lower infectious morbidity associated with its use. This shows that the administration of beta-lactam antibiotics is more effective in preventing the incidence of post-infection caesarean section compared to other antibiotics (Harris et al., 2019; Kawakita et al., 2018).

While the study by Assawapalanggool et al, which compared the effectiveness of two types of beta-lactam antibiotics, namely ampicillin and ceftriaxone, stated that both of them had the same effectiveness in preventing complications of postoperative surgical site infection complications of cesarean section. It was said that the incidence of, both incisional and surgical site infections organ / space surgical site infections, was not statistically significant in the two groups, respectively (RR, 0.23; 95% CI 0.03-1.78) and (RR, 1.62; 95% CI 0.83–3.18) (Assawapalanggool et al., 2018).

Through this literature review, it was also found that the use of a combination of non-beta-lactam antibiotics with standard beta-lactam antibiotics can increase effectiveness in reducing the risk of infection in the surgical area. Standard prophylactic antibiotics have been shown to reduce the rate of infection of the surgical area after cesarean section, along with rates of serious maternal complications and mortality. Research by Tita, et al. demonstrated that administering broad-spectrum prophylactic antibiotics with the addition of azithromycin as an adjuvant for cesarean section in women with an increased risk of infection, safely reduces infection rates and maternal use of health care resources without increasing the risk of adverse neonatal outcomes. Addition of azithromycin to standard prophylactic antibiotics significantly reduces the frequency of non-elective post-caesarean infections. The risk of serious maternal side effects, including readmissions, was lower than in the group not given azithromycin supplementation. The risk or side effect of the neonate did not increase in the azithromycin-added group. This study focuses on azithromycin use because this type of antibiotic includes

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ureaplasma organisms, which are more frequently associated with post-caesarean section infection than anaerobes when specific cultures are performed, and because they have been associated with a reduced risk of surgical wound infection and endometritis. (Tita et al., 2016)

This is in line with research by Jyothi, et al. which stated that the rate of surgical site infection was higher in the group receiving cefazolin with the placebo, than in the group receiving cefazolin with azithromycin. The duration of hospital stay was significantly longer in the placebo group because of the need for additional antibiotics and indirectly increasing the cost burden to patients. This study by Jyothi, et al. Was planned to evaluate the effectiveness of adding a single-dose broad-spectrum antibiotic - azithromycin to cefazolin as a standard prophylactic antibiotic - for cesarean section (Jyothi et al., 2019). Four RCT studies compared the use of narrow-spectrum prophylactic antibiotics (first-generation cephalosporins or ampicillin) with broad-spectrum antibiotics, which have added agents from different antibiotic classes such as gentamicin, metronidazole, and azithromycin. Prophylactic antibiotics were associated with a statistically significant reduction in rates of infection, endometritis, and wound infection when compared with a narrow spectrum.

Meanwhile, Valent et al. Mentioned the effectiveness of giving a combination of cephalexin and oral metronidazole after surgery in reducing the risk of infection in the surgical area, preceded by the provision of standard preoperative prophylactic antibiotics (Valent et al., 2017). From these three studies, it can be considered the use of other types of antibiotics as adjuvant prophylactic regimens.

Timing of Administration of Prophylactic Antibiotics

Provision of perioperative prophylactic antibiotics for sectio caesarea is more effective in preventing the incidence of infection in the surgical area than postoperative administration. This is explained in the study of Sway et al., where the incidence of surgical site infection was higher in the group receiving postoperative antibiotics (9.3%) than in the group receiving preoperative prophylactic antibiotics (4.0%). Sway, et al. also argued that the administration of prophylactic antibiotics was the main reason for the lower infection rate and that these data provide strong evidence that many of the infectious problems faced in the study population would be reduced by administering antibiotic prophylaxis prior to incision. However, the limitation of this study is that more than one antibiotic class is used, including ceftriaxone, a combination of ceftriaxone and metronidazole, and a combination of ampicillin and metronidazole (Sway et al., 2020).

Therefore, we believe that the timing of antibiotic therapy is likely the main reason for the lower infection rates seen in Thika and that these data provide strong evidence that many of the infectious problems encountered in this population will be reduced by prior antibiotic prophylaxis. to the incision.

The antibiotic cefazolin at a dose of 1 gram can be given intravenously 30-60 minutes before the skin incision to achieve the highest concentration in the tissue to effectively prevent wound infection and with a half-life of about 1.8 hours. The greatest therapeutic effect occurs when antibiotics are given just before or at the same time when bacterial contamination is maximal and tissue trauma occurs. Several studies mention that prophylactic antibiotics are injected after clamping the umbilical cord so that it does not reach the fetal circulation. However, recent research shows that giving the drug before skin incision will significantly reduce the incidence of infection in the mother without harming the baby (Jyothirmayi et al., 2017).

Pre-incision prophylactic antibiotics have been shown to protect women from surgical wound infection and fever and significantly reduce the length of stay. This was demonstrated in a study examining the optimal timing of prophylactic antibiotics and assessing the amount of antibiotics crossing the placental barrier. This research was conducted in India which was conducted on 1,106 women who were divided into two groups; 533 mothers received antibiotics before skin incision (pre-incision) and 543 mothers received antibiotics after umbilical cord clamping (post-incision). This study found that intravenous prophylactic antibiotics are effective for mothers who are going to undergo caesarean section before skin incisions and reduce the overall incidence of postoperative infectious morbidity in mothers. And in this study we also found that no significant side effects were seen in neonates when intravenous cefazolin was given before the skin incision. The amount of antibiotics that accumulates in the umbilical cord blood is only 2-3% (Jyothirmayi et al., 2017).

In a study by Purbadi, et al. who used a single dose of cefazolin given before incision, in line with the conclusions of a systematic review that also supports the administration of cefazolin as the prophylactic antibiotic regimen of choice before incision. In the last decade, through the development of studies related to prophylactic antibiotics www.turkjphysiotherrehabil.org
and the timing of appropriate administration of cesarean section, a systematic review by Mackeen, et al. stated that from 10 recent studies concluded that the use of prophylactic antibiotics before incision was superior to that of administration after cord clamping. (RR 0.57 (95% CI 0.45-0.72)).

V. CONCLUSION

The high rate of delivery by the sectio caesarea method will increase the high likelihood of infection-related wound complications in women undergoing cesarean section in Indonesia. Complications of infection in the area of infection after caesarean section are still a problem because they are associated with significant maternal mortality and morbidity. Based on the critical analysis that has been carried out, from the 11 articles obtained, it can be concluded that the recommended prophylactic antibiotics are the beta-lactam group, namely the first-generation cephalosporin (cefazolin) and the combination of clindamycin with the aminoglycoside group if allergic to beta-lactam. The addition of adjuvant antibiotics in addition is also recommended, the choice of adjuvant antibiotics such as azithromycin, gentamicin, and metronidazole. In addition, the recommended time for prophylactic antibiotics is 30-60 minutes before the skin incision is performed.

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