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EFFECTIVENESS OF COMBINATION OF CEFAZOLINE AND AMINOGLYCOCIDES IN OPEN FRACTURE, A CASE REPORT STUDY

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ABSTRACT

Open fractures are a serious problem because they can cause complications to disability. The biggest cause of open fractures is accidents. Open fractures are classified into three groups according to Gustilo and Anderson, namely Grade I, Grade II and Grade III. Proper handling of open fractures can minimize complications that may occur, one of which is infection. Antibiotic prophylaxis is one of the mainstays of open fracture management and needs to be prescribed as soon as possible because early antibiotics reduce the infection rate in open fractures. For this reason, it is very important to determine the choice of antibiotics used.

INTRODUCTION

An open fracture is a fracture in which a tear in the skin allows direct contact of the fracture site or fracture hematoma with the outside world where this condition is very dangerous because it can cause infection in the fracture area.[1,2] If this occurs while the patient is in hospital, it is called a nosocomial infection. It is estimated that 1 in every 120 people under the age of 65 will experience a fracture and 3% of these fractures are open. Three to six million fractures occur each year in the United States.[1] Research data in Indonesia shows that the incidence of open fractures is more common in men aged 36-45 years. As for the type of fracture, most are open fractures and the location of the most fractures is in the tibia. Accidents are the biggest cause of open fractures.[3] The classification of open fractures as in table 1 is divided according to Gustilo and Anderson into three groups, namely Grade I,

Grade II and Grade III where Grade III is further divided into Grade IIIA, Grade IIIB, and Grade III C based on the severity of the soft tissue.[2,4]

Table 1: The Gustilo and Anderson classification (Jorge-Mora et al., 2022).

	I	II	III-A	III-B	III-C
Energy of mechanism	Low	Moderate	High	High	High
Wound size	<1 cm	>1 cm	Usually >10 cm	Usually >10 cm	Usually >10 cm
Soft tissue injury	Low	Moderate	Extensive	Extensive	Extensive
Contamination	NO	Low	Severe	Variable	Variable
Conminution/ Fracture pattern	No/ Simple	Some/ Simple	Severe/ Complex	Severe/ Complex	Severe/ Complex
Soft tissue coverage	Yes	Yes	Yes	No, requires reconstructive procedure	Variable
Vacular injury injury	No	No	No	No	Yes, require reparation

Early management using prophylactic antibiotics is very important to prevent postoperative infection. The results of previous studies showed that the most common pathogen involved in the incidence of open fractures is staphylococci which are gram-positive bacteria but it is not possible for gram-negative bacteria to also be involved in this condition.[4] Antibiotic prophylaxis is one of the mainstays of open fracture management and needs to be prescribed as soon as possible because early antibiotics reduce the infection rate in open fractures. The British Orthopedic Association recommends giving antibiotics within 3 hours of the injury. The British Orthopedic Association (BOAST 4) recommends the use of Co-amoxiclav (1.2 g) or Cefuroxime (1.5 g) every 8 hours and continue until wound debridement. Clindamycin 600 mg every 6 hours can be used if there is a penicillin allergy. Another validated recommendation is the use of cefazolin and gentamicin or piperacillin/tazobactam for 24 hours after debridement.[4]

CASE REPORT

In this case, it is known that patient data aged 56 years, 65 kg, was admitted to the hospital due to an accident so that the patient received 4 treatments including debridement plus external fixation (30/3/2020), debridement (2/4/2020), skin graft 3% redebridement (18/4/2020 and 24/4/2020) received antibiotic therapy cefazolin 3 times a day 1g (4 days) (30/3/2020-2/4/2020), Mikacin 750mg (1 day), 1500mg every 12 hours (3 days)), 500mg every 8 hours (2 days), 500mg every 12 hours (1 day) (30/3/2020-5/4/2020), Ceftriaxone 1g

every 12 hours (4 days) (2/4/2020-5/4/ 2020). The profile of antibiotic therapy obtained by patients during hospitalization can be seen in table 2 below.

Table 2: Patient antibiotic therapy profile.

Antibiotic therapy	Date						
	30/03	31/03	01/04	02/04	03/04	04/04	05/04
Cefazolin 3x1 g	v	v	v	v			
Mikacin 750 mg	v						
Mikacin 2x1500 mg		v	v	v			
Mikacin 3x500 mg					v	v	
Mikacin 2x500 mg							v
Ceftriaxone 2x1 g				v	v	v	v

DISCUSSION

An open fracture is an injury in which bone fractures and/or hematoma fractures are exposed to the external environment through trauma to the soft tissues and skin.[5,6] There are several grades of open fractures, including grades I, II, IIIA, IIIB, and IIIC.[7–10] In this case, the patient was diagnosed with an open fracture cruris 1/3 medial Grade IIIB where the infection rate of open fracture IIIB was 10-50%.[7] Open fracture IIIB contains gram-positive and negative bacteria.[11,12] Antibiotics recommended for open fracture IIIB are Cephalosporin generation I (Cefazolin 1-2g IV every 8 hours) Aminoglycoside combination for 24-72 hours.[5–7,10,11,13–18] From this case, it can be seen that the antibiotic used was a combination of cefazolin and micasin for 5 days, followed by a combination of ceftriaxone and micacin for 4 days. On 02/04 it was seen that the patient received 3 combinations of antibiotics, namely cefazolin, ceftriaxone and micasin. According to treatment guidelines, a combination of cefazolin (a class I cephalosporin) and mycacin (an aminoglycoside) is appropriate. The choice of ceftriaxone, which is an antibiotic from the third generation cephalosporin group, may be aimed at broadening the scope of bacterial pathogens that have the potential to cause infection, whereas the third generation cephalosporin group has a wider spectrum of activity than other generation of cephalosporins and is active against Gram-negative organisms, including many significant Enterobacteriaceae. and is also highly active against streptococci.[19] The effectiveness related to the use of ceftriaxone is not discussed because the use of ceftriaxone is a follow-up therapy where in this case report the researcher wants to focus more on the selection of prophylactic antibiotics used, namely the combination of cefazolin and micasin.

Regarding the effectiveness of prophylactic antibiotics used, from several studies comparing cefazolin monotherapy with cefazolin plus an aminoglycoside in retrospective gustillo III open fractures, infection occurred in 6 of 39 patients (15%) in the cefazolin monotherapy group and 15 of 95 patients (16%) cefazolin plus aminoglycoside group (p-value=1,000), 8 of 53 patients (15.1%) (RR: 0.38 AR: 24.9%) cefazolin monotherapy group and 6 of 15 patients (40%) cefazolin plus aminoglycoside group.[20,21] The results of the analysis of several studies showed that there was no significant difference between cefazolin monotherapy and cefazolin plus an aminoglycoside in reducing infection in gustillo III open fractures. [20–22]

According to the study of Messner, et al 2017, in a meta-analysis of open fractures of Gustilo III, the infection rate (21.3%, 95% CI: 13% -31%) duration of antibiotic treatment of more than 72 hours was not significantly different compared to those with less of 72 hours (17.7%, 95% CI: 12.5% - 23.5%) (p = 0.39). Further subgroup analysis showed that antibiotics with shorter duration of administration (24–48 h) were also equivalent to duration of administration of more than 72 hours in infection rates.[23]

CONCLUSION

The conclusion from some evidence related to the case report is that the addition of aminoglycosides is not necessary to prevent infection in gustilo III open fractures because there is no significant difference between cefazolin monotherapy and its duration should not be more than 72 hours. But this also needs to be adjusted to what bacteria have the potential to cause infection.

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