Use of prophylactic antibiotics for debridement surgery in burn patients – A retrospective surveillance

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Abstract

Background

Burn injury is trauma with a high risk of infection. Debridement is a method that can be used to prevent and decrease the incidence of infection and accelerate wound healing. To minimize surgical site infection, the use of prophylactic antibiotics was considered in debridement.

Objective

The main objective of this study was to characterize the usage of prophylactic antibiotics for debridement in burn patients, including the selection, dose, and route of administration. The other objective was to quantitatively calculate the use of prophylactic antibiotics using ATC/DDD. (Anatomical therapeutic chemical/Defined Daily Dose)

Method

This was a retrospective study in burn patients admitted to the Government Cuddalore Medical College (GCMC), Chidambaram between 2019 and 2022.100 burn patients meet the inclusion criteria enrolled in this study. There were three prophylactic antibiotics used for debridement in this study. All prophylactic antibiotics were given intravenously.

The most common prophylactic antibiotics were ceftriaxone, meropenem, cefoperazone. Cefoperazone, and meropenem were used as therapeutic antibiotics to treat burn infection and continued as prophylactic before debridement surgery. ceftriaxone and cefoperazone were the most antibiotics that comply their dose with the guideline.

Result

Out of the total of (Defined Daily Dose) DDD/100 operations ceftriaxone was the highest consumed.

The mortality rate in our study was very less. For those who survived, there was a significant correlation between % TBSA and length of stay also debridement frequency.

Conclusion

Our study concluded that there was decrease in the infection and mortality rate after the administration of prophylactic antibiotics in debridement surgery for burn patients but improvements were needed to use prophylactic antibiotics more precisely regarding quantity and choice of the type of antibiotics.

Key Words

Prophylactic antibiotics, Debridement, Burns, ATC/DDD.

I. INTRODUCTION

A burn is one of the severe injuries with high morbidity and mortality, especially when the burn size is over 40% in adults [1]. Burn usually causes skin disruption, which allows pathogenic bacteria to easily invade the body and leads tomild or high risk of infection [2]. Burn patients were more susceptible to infection compared to other injuries. A study by Belba et al, reported that the prevalence of infection in burns was 12% and the colonization was 44% [3]. One of the standard therapies of burn patients in the acute phase to prevent infection is early wound excision or debridement [4]. A method to reduce colonization of pathogenic bacteria and decrease infection risk in burn patients is debridement.

Debridement is a commonly used surgical procedure to remove necrotic tissue. Necrotic tissue due to burns is a factor that inhibits wound healing and provides a good place for nosocomial bacterial growth. The main purpose of early debridement was to accelerate wound healing, reduce systemic infection and other nosocomial infection, length of stay in the hospital, and improve survival. Most studies reported that early excision within 24-48 hours after burns was significantly associated with reduced blood loss, systemic infection, length of stay, mortality, and increased skin graft. However, a reduction in mortality may only occur in burn patients without inhalation trauma.

Debridement was applied in partial-thickness and full-thickness of burns that was not completely healing within 14-21 days. Debridement was classified as clean-contaminated surgery with a high risk of surgical site infection. Therefore, to reduce the incidence of surgical site infection after debridement surgery and its complication, prophylactic antibiotics administration was considered as effective. The pathogens related to a specific surgical procedure; site of burn should be considered when selecting a prophylactic antibiotic. Antibiotics with a broader spectrum, such as aminoglycosides (kanamycin, amikacin) should not be used for prophylactic antibiotics. In Indonesia, it has been reported that compliance of antibiotics with the guidelines was poor. Only 6.1% of used in orthopedic surgery met The National Guideline for Antibiotic Use in Indonesia. Ceftriaxone was one of the most common antibiotic prophylaxes. To date, there were no established guidelines to support the use of prophy- lactic antibiotics for debridement surgery in burn patients. There is still limited information regarding selecting prophylactic antibiotics for debridement and the quantity of DDD units. High DDD units will indicate the uncontrolled level of antibiotic consumption. The purpose of this study was to obtain the appropriateness of prophylactic anti- biotics for debridement based on the selection, dose, route of

administration and to obtain the defined daily dose (DDD) for every 100 operations of prophylactic antibiotics.

II. MATERIALS AND METHODS

Study design

This study was an observational retrospective using medical records of burn patients admitted to the Government cuddalore medical college and hospital (Chidambaram) between 2019 to 2022. This study analyzed the appropriateness of prophylactic anti-biotics for debridement surgery including type,dose, and route of administration, and unit of antibiotics as a defined daily dose (DDD).

Inclusion and exclusion criteria

This study's inclusion criteria were: 1) burned patients aged more than 18 years old, 2) partial or full-thickness burn, and 3) debridementsurgery was performed at least once during hospitalization. The exclusion criteria were incomplete medical records, including unclearly written of the type, dose, and route of administration of the prophylactic antibiotics.

III. Data analysis

Baseline demographics including sex, age, % Total Body Surface Area (TBSA), depth of burns, length of stay, and mortality were recorded. The numerical data such as percentage of TBSA, age, length of stay, the dose of prophy-lactic antibiotics was expressed as mean ± standard deviation. The categorical data such as sex, mortality, and inhalation trauma were presented as a percentage. American Society of Health-System Pharmacist (ASHP) therapeutic guideline was used to evaluate the selection, dose, and route of administration of pro- phylactic antibiotics for perioperative surgery.

The use of prophylactic antibiotics was quantitatively analyzed as the defined daily dose (DDD) per 100 procedures of debridement using the anatomical therapeutic chemical (ATC). In this study, we used DDD and DDD-100 operation days to represent prophylactic antibiotics. The DDD is a drug utilization figure that is compared to the WHO's DDD standard. The latter is a measurement unit for the assumed daily average maintenance dose of a drug used for its primary indication in adults. DDD per 100 operation days was only analyzed in burn patients who survived until discharged from the hospital. Each burn patient has undergone more than one debridement surgery. The se- lection and the dose were presented as a descriptive report. According to the Anatomical Therapeutic Chemical (ATC) classification for antibacterial for systemic use, the antibiotics were divided into five groups (J01) in this study [5].

Table 1 Demographic Data

Variables	n=180
Sex, n (%)	
Female	54 (30)
Male	126 (70)
Age (years)	
Range	19-81
Mean ± SD	44.3 ± 14.8
TBSA (%)	
Range	1-94
Mean	32.7 ± 23.2
TBSA > 20%	56 (62.2)
Depth of Burn	
Grade IIAB	104(58)
Grade III	76 (42)
Length of stay (days)	
Range	3-55
Mean ± SD	16.1 ± 10.0
Cause of Burns	
Fire	126 (70)
EIHV	38(21)
Scald	16 (9)
Mortality	
Survive	120(67)
Death	60(33)
Inhalation Trauma	
Yes	76(42.2)
No	104(57.8)

The following equation was used for calculation of DDD per 100 operation days.

$$\textbf{DDD 100/operation days} = \frac{\textbf{Antibiotics(gram)x100}}{\textbf{DDD WHO (gram)xLOS}}$$

DDD WHO = Defined Daily Dose WHO;

LOS = Length of stay.
The DDD per patients was calculated as follow:

$$\textbf{DDD per patients} = \frac{\textbf{Total DDD}}{\textbf{Number of patients}}$$

To determine the accuracy of the dose of pro-phylactic antibiotics, the following equation is used:

$$\frac{\textbf{The right amount of antibiotic dose}}{\textbf{The total amount of antibiotic}} \textbf{x100}\%$$

We used Spearman correlation to correlate the percentage of TBSA with length of stay and debridement frequency, and we used bivariate analysis (chi-square test) to associate variables (age, TBSA, and inhalation trauma) with developing mortality in burn patients. The data were stated to correlate with the Spearman correlation and have an association through the Chi-square test if the p-value was less than 0.05. The statistical strength of correlation is stated to be very weak if the correlation coefficient (r) between 0.0- < 0.2, weak 0.2- < 0.4, moderate 0.4- < 0.6, strong 0.6- < 0.8, and very strong 0.8-1.0. All statistical analyzes were performed using the SPSS version 16 software program.

IV. RESULTS

Demographic profile

A total of 180 medical records of burn patients were analyzed in this study. Of these, 126 (70%) were men with a mean of 44.3 years.The most frequent cause of burns was fire witha percentage of 70. The length of stay had a mean of 16.1 days (3-55). The most frequent outcome was hospital discharge, occurring in 120 (67%) of the burned patients. We found 42.2% of burn patients had trauma inhalation.Detailed information was shown in Table 1. Spearman correlation in burn patients who survived between the percentage of TBSA and length of stay also the percentage of TBSA anddebridement frequency were shown in Table 2.We found a positive correlation between the percentage of TBSA with length of stay and debridement frequency.

Table 2 Spearman correlation among variables

No	Variables	Mean ± SD	P-Value	r
1.	Total Body Surface Area (TBSA) %	20.7±14.9		
2.	Length of Stay (Los)	17.9± 9.8	0.018	0.311
3.	Debridement frequency	2.3 ±1.0	0.014	0.323

Profile of prophylactic antibiotics

The most frequent prophylactic antibiotic ceftriaxone (11%). All prophylactic antibiotics were given with a mean of more than one gram. Detailed information of profile and dose of prophylactic antibiotics for debridement were shown in Table 3.

Table 3 Profile and dose of prophylactic antibiotics for debridement

No	Antibiotics	Total*	Percentage (%)	Dose range (g)	Mean±SD (g)
1.	Ceftriaxone	20	64.5	1-2	1.7±0.4
2.	Cefoperazone	3	9.6	1-2	1.3±0.5
3.	Meropenem	8	25.8	1-2	1.1±0.3

*the total was counted from 90 burn patients who undergone debridement surgery.

Number of DDD of prophylactic antibiotics

According to the guideline, all prophylactic anti- biotics were given intravenously. Ceftriaxone complies 100% with the guideline among burned patients. Furthermore, ceftriaxone was the most prophylactic antibiotics that comply with the guideline75%, respectively (Table 4). A total of DDD/100 operations of prophylactic antibiotics was 1.3, with the highest DDD was Ceftriaxone (1.20 DDD/100 operations). Table 5 showed the number of DDD of each antibiotic.

Table 4 Frequency of antibiotic Prophylactic based on the guideline

No	Antibiotics	No. of Patients (%)	Dose (%)
1.	Ceftriaxone	16(100)	56(75)
2.	Cefoperazone	3(0)	3(0)
3.	Meropenem	4(0)	8(0)

Table 5 Number of DDD/100 operations of prophylactic antibiotics

NO	Antibiotics	ATC Code	DDD WHO (gram)	Total dose	DDD	DDD/100 Operations
1.	Ceftriaxone	J01DD04	2	25	12.5	1.20
2.	Cefoperazone	J01DD12	4	3	0.75	0.07
3.	Meropenem	J01DH02	3	1	0.33	0.03
			Total	29	13.58	1.3

*DDD: defined daily dose. *The number of DDD was calculated only in survived patients until discharge.

Association of mortality

To analyze the association percentage of TBSA, age, and inhalation trauma to mortality, bivariate analysis (Chi-square) was performed as shown in Table 6.

Table 6 Chi- Square Analysis to mortality

No	Variables	Death		p-Value	OR	CI 95%
		Yes, n (%)	No, n (%)			

1.	Age (years)	> 60	8 (53)	7 (47)	0.072	2.753	0.890-8.520
		< 60	22 (29)	53 (71)			
2.	TBSA (%)	>20	29(52)	27(48)	0.000*	35.44	4.530-277.355
		<20	1(3)	33(97)			
3.	Inhalation trauma	Yes	20 (53)	18 (47)	0.000*	5.309	2.033-13.865
		No	9 (17)	43 (83)			

*Statistically significant (p-value < 0.05).

V. DISCUSSION

Based on demographic data, males are higher than females with a ratio of F:M was 1:3. All burn patients in this study included second and third-degree burns, thus requiring debridement. Forty-two percent of burn patients in our study had inhalation trauma on admission. Burn patients with inhalation injury were significantly longer in hospitalization than those without inhalation injury. This study found a significant correlation between Total Body Surface Area (TBSA) and length of stay (LoS) and TBSA and debridement frequency.

The inflammation process was extensively higher in TBSA, more than 20% characterized by the release of inflammatory mediators such as IL-6, TNF-α, and Phagocytic cells. If the releasing of inflammatory mediators simultaneously continues, it will suppress immunity and leads to severe infection. Burn patients with severe infection cause the medication was more complex and prolonged the hospital stay. The higher the percentage of TBSA, the bigger the burned body area. Therefore, to stimulate new tissue and promote wound healing, debridement surgery was more likely to be performed.

Infection in the wound can occur during treatment in the hospital caused by the hospital environment, medical equipment, and surgery. A study by Junior et al, stated that on the first day after burns, as many as 96% of patients did not find any bacterial growth and only found it on the fifth day after burns. Several studies have been evaluated the effectiveness of pro-phylactic antibiotics for debridement in burn patients. However, the results were still controversial. Some burn surgeons recommended using routinely prophylactic antibiotics, while others did not. A single dose of pre-operative antibiotic decreases the possibility of surgical site infection, especially for auto-grafting procedures. However, the risk and benefits of pre- operative antibiotics for newer minimally invasive debridement and grafting techniques are lacking.

The antibiotic should be selected based on the antibacterial spectrum and the indication. In clean- contaminated procedures, bacteria causing surgical site infections are like those caused by skin flora in clean surgery, plus gr- am-negative rods and enterococci. Ceftriaxone, a first-generation cephalosporin, is used to prevent such infections under the Indonesia Ministry of Health guideline. In our study, all prophylactic antibiotics were administered intravenously as a single dose. Administration of a single dose in a short time relatively achieves a high concentration above minimum inhibitory concentration (MIC) to inhibit infection during or after surgery compared to infusion in an extend- ed period. The advantages of the single-dose prophylactic antibiotics were cheap and relatively small errors.

After the administration of single dose 1 gram of ceftriaxone intravenously for debridement surgery in burn patients the mean duration of MIC (68 mg/L) for Pseudo- monas aeruginosa was only 1.35 hours ranged from 2.25 to 8.5 hours. These findings suggested re-dose of beta-lactams by continuous infusion to minimize infection risk after debridement in burn patients. The administration of prophylactic antibiotics should be repeated if the duration of surgery more than two half-lives after the first dose to maintain their concentration above MIC. We could not evaluate the second dose of prophylactic antibiotics during debridement because there was no information.

Overall, in this study, the antibiotic use was 1.3 DDD per 100 operation days meaning that on average, there were 0.13 WHO's DDD per patient per day or 1.3 WHO's DDD for 100 patients per day. This indicates that 1.3% of the patients received a DDD of a prophylactic antibiotic per day. The commonly used pro-phylactic antibiotic in our study was ceftriaxone. Based on number of DDD/100 operations, ceftriaxone was the highest consumed with 1.20 DDD/100 operations. It indicated that every operation or debridement procedure, the average use of ceftriaxone 1.20 times from the WHO standard DDD of ceftriaxone, 2 grams. Ceftriaxone is third generation of cephalosporin, actively against gram positive bacteria such as S. aure- us, Staphylococcus epidermidis, and Escheri- chia coli. These bacteria are normal flora in human skin, but cause infection in opened skin. The dose of ceftriaxone in our study was 1 gram. Based on ASHP, the dose of cefazolin for perioperative prophylactic was 1 gram.

We found the DDD value was smaller than the results of several studies because the number of antibiotics was only measured in burn patients' debridement surgery, while all surgical procedures were used in other studies. The total patient's length of stay was 1.038 days, and it was shorter than those in a study by Herawati et al, 1868 days. Based on DDD, the number of prophylactic antibiotics given in this study was smaller than that determined by WHO, as shown in Table 5. It indicates that the level of prophylactic antibiotics for debridement procedures in terms of quantity is quite good.

One gram of ceftriaxone at anesthesia induction, followed by a repeat dose after initiation of cardiopulmonary bypass provides sufficient drug concentrations to target most pathogens associated with surgical site infections. A study by Ramos et al, stated in burn patients without administration of prophylactic antibiotics, ten from thirty-five surgical procedures (28%) was confirmed as bacteremia's.

Burn patients with TBSA more than 40% was significantly as a risk factor to bacteremia with RR 3.78 (0.93-15.33). However, one study reported that prophylactic antibiotic should not be routinely recommended in debridement surgery. Bacteria colonizing the burn wound or before debridement surgery may not be susceptible to ceftriaxone, but the administration of broad-spectrum antibiotics to cover all possible bacteria or microorganisms may develop resistant organisms and overgrowth fungi. Therefore, prophylactic antibiotics' risks and benefits should be weighed carefully to minimize the adverse effects of antibiotics.

As much as 9.5% of ceftriaxone was used as prophylactic, 75% of its dose comply with the guideline. Several studies recommended using ceftriaxone as prophylactic antibiotics perioperative, especially in surgery that suspected gram-negative

bacteria contamination [6]. A study by Alemkere reported that ceftriaxone was the most used as prophylactic antibiotic (85%) in the surgical ward of Nekemte hospital, Ethiopia. However, surgical antibiotic adherence was significantly lower than the guideline recommendation [7]. The effectiveness of cefazolin or ceftriaxone to prevent surgical site infection in clean surgeries was remained unclear. One study reported there was no differences in the rate of surgical site infection in patients receiving two grams of cefazolin or ceftriaxone as perioperative antibiotic in orthopedic surgeries.

We found three antibiotics to be used for pro-phylactic debridement, including Ceftriaxone, cefoperazone, and meropenem that were not recommended as prophylactic antibiotics for surgery in several guidelines, including ASHP. These antibiotics were used as therapeutic antibiotics for nosocomial pneumonia for burn patients in our study. Meropenem is the highly potent broad-spectrum antibiotics. They were used as alternatives if the bacteria are resistant to cephalosporins. Ceftriaxone, meropenem are not recommended for specific gram-positive skin flora. Prophylactic antibiotics that were not appropriate from the type, dose, and administration route caused an increase in antibiotics resistance. Resistance can be defined as no bacterial growth inhibition by systemic administration of antibiotics at their minimum inhibitory level or standard dose.

In the last few decades, there has been an increase in the prevalence of multidrug-resistant organisms (MDROs) worldwide. Currently, clinicians face an increasing number of

P. aeruginosa and A. baumanii infections resistant to nearly all beta-lactam, aminoglycosides, and quinolone antibiotics. A study by Aisyah et al, stated that the profile of bacteria found in burn patients who were treated at Dr. Soetomo from February to May 2018 was MDRO bacte- ria including P. aeruginosa (11%), Klebsiella pneumonia (6%), A. Baumannii (12%), as well as extended beta-lactamase spectrum (6%). Other results where the sensitivity level for cefoperazone-sulbactam (33%), meropenem (33%).

Other results in this study were TBSA above 20%, age over 60 years, and inhalation trauma significantly affecting mortality in burn patients (p-value <0.05). Our study was like the study by Chung et al, stated that age and per- centage of TBSA were significant risk factors for mortality. In our study, out of 180 patients, 60 of them (33.3%) died during their hospitalization. Of the 60 patients who died, 30 of them (50%) were accompanied by acute kidney injury. This study's mortality rate was very Less. The leading cause of death was septic shock, multiple organ failure (MOF), and acute respiratory distress syndrome (ARDS).

There were some limitations in our study, including the retrospective design and a limited number of samples. Time to administer prophylactic antibiotics and whether a second dose was given during debridement were unavailable during data collection. Furthermore, we did not observe the efficacy of prophylactic antibiotics to minimize surgical site infection after debridement. Further research was required to determine if prophylactic antibiotics confer benefits in a burn patient population's debridement surgery.

VI. CONCLUSION

A significant improvement in the use of prophylactic antibiotics for debridement in burn patients is required. Every hospital must publish an antibiotic use guideline or clinical pathway for every type of surgery including debridement surgery. To prevent the occurrence of microbial resistance, we recommend the selection of narrow-spectrum antibiotics. As a result, the findings of our study are essential for future policy decisions in this field. Pharmacists or other health care professionals should elaborate on each other to consider the administration of prophylactic antibiotics for debridement in burn patients to prevent the high risk of infection.

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