EVALUATION OF ANTIBIOTIC USE AND BACTERIAL PROFILE IN BURN UNIT PATIENTS AT THE DR. SOETOMO GENERAL HOSPITAL

ÉVALUATION DE L'UTILISATION DES ANTIBIOTIQUES ET DE L'ÉCOLOGIE DANS LE CTB DE L'HÔPITAL DR SOETOMO

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SUMMARY. The high inaccuracy of antibiotic prescribing in Dr. Soetomo General Hospital Surabaya, Indonesia, is one of the factors triggering the increasing prevalence of antibiotic-resistant pathogenic bacteria. The World Health Organization (WHO) showed that bacterial resistance to antibiotics was a threat to people's health around the world. Burn injuries are susceptible to infection and need appropriate antibiotics. The purpose of this study was to obtain a germ map for our burn patients and to evaluate the antibiotic therapy that had been used to treat them. This was a descriptive observational study, conducted in the Burn Unit at the Dr. Soetomo General Hospital. The study used data from burn patients who were treated there from February to May 2018. The patients' medical records, records of drug usage (antibiotics) and culture results data (bacterial sensitivity test for antibiotics) were examined. Total antibiotic usage was calculated using the Defined Daily Dose (DDD) method per 100 days. The quality of antibiotic usage was assessed using the Gyssens method. Bacterial profile was obtained from culture swab. According to our findings, the most widely used antibiotic is *ceftazidim* with DDD / 100 days of 22.25. Based on the qualitative analysis using the Gyssens method, 33.3% were in category VI-0. The most common bacteria obtained from the swabs were *Bacillus cereus* and *Acinetobacter baumanni*, found in 12% of the patients. Antibiotics are still not used wisely in the Burn Unit at the Dr. Soetomo General Hospital.

Keywords: antibiotics, resistance, profiles of germs, burn

RÉSUMÉ. *La grande fréquence des antibiothérapies inappropriées est un des facteurs de la forte prévalence de bactéries résistantes dans l'hôpital Dr Soetomo de Surabaya (Indonésie). L'OMS a montré que la résistance bactérienne représentait un danger mondial de santé publique. Les patients brûlés sont particulièrement à risque d'infections, nécessitant une antibiothérapie appropriée. Cette étude prospective observationnelle avait pour but d'étudier l'écologie des infections dans le CTB de cet hôpital et les antibiotiques utilisés, entre février et mai 2018. Les dossiers des patients, de la pharmacie (antibiotiques) et de la bactériologie (germes et antibiogrammes sur cultures d'écouvillons) ont été revues. La consommation d'antibiotiques a été exprimée en Dose Définie Journalière (DDJ) pour 100 jours-patients. La qualité d'utilisation des antibiotiques était évaluée selon la méthode de Gyssens. La ceftazidime était l'antibiotique le plus utilisés (22,25 DDJ/100 j-pat.). Un tiers des prescriptions étaient dans la catégorie VI-0 de Gyssens. Les bactéries les plus fréquentes étaient* B. cereus *et* A. baumannii *(12%). Les antibiotiques ne sont toujours pas utilisés* larga manu *dans le CTB de l'hôpital Dr Soetomo.*

Mots-clés : *antibiotiques, résistance, écologie bactérienne, brûlés*

Introduction

Burns are a tissue damage condition caused by thermal trauma.[1] In 2014, the World Health Organization (WHO) estimated that each year there were 265,000 deaths worldwide due to burns. In Bangladesh, Columbia, Egypt and Pakistan, 17% of children with burns suffer from temporary disability and 18% suffer permanent disability. In Nepal, burns are the second leading cause of injury, with 5% disability.[2]

A previous study conducted by Saputro (2011) on 181 burn injury patients in the Dr. Soetomo General Hospital showed that 24 patients died.[3] In that study, mortality rate was 68.4% for patients with >60% Total Body Surface Area (TBSA) burned, 7.4% for patients with 20-60% TBSA, and 2.7% for patients with <20% TBSA. Another study conducted by Bowo (2016) at the Hasan Sadikin Hospital found that 71 out of 164 burn injury patients died.[4] The main cause of death was acute respiratory distress syndrome (53%) and sepsis (42%). Based on TBSA, mortality rate was 92% for patients with >60% TBSA, 79% for patients with 51-60% TBSA, 50% for patients with 31-50% TBSA, 17% for patients with 15-60% TBSA, and 30% for patients with <15% TBSA.

In the treatment of burn patients, antibiotic therapy is needed because of the high rate of infection. However, careful

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consideration is necessary when prescribing antibiotics for burn patients in order to avoid therapy failure that can cause resistance. An examination of antibiotic resistance in burn patients in the Dr. Soetomo General Hospital Burn Unit showed that *cefotaxime* was the most resistant antibiotic, whereas *ampicillin* was the least resistant.[3] Some common causes that contribute to the development of antibiotic resistance are inappropriate use of antibiotics, inappropriate dosages, and inadequate use of time.[5] The criteria for rational antibiotic use are the right type, right dose, right method and duration; moreover, that it has been proven that the medicine used is safe for patients and the price is affordable.[6] Based on the results of research by Hadi et al (2010) at two general hospitals in Indonesia (Dr. Soetomo and Dr. Kariadi General Hospital), it was found that antibiotic prescribing rates had no indication for infection.[7] The high inaccuracy in prescribing antibiotics is one of the factors that has triggered the increasing prevalence of antibiotic-resistant pathogenic bacteria.

In the effort to control the spread of antibiotic-resistant bacteria, in 2014 WHO and Centers for Disease Control and Prevention (CDC) recommended that all hospitals implement antibiotic stewardship programs.[8] Antibiotic stewardship is a collection of coordination strategies to encourage a wise use of antibiotics through optimal selection of classes, doses and duration of antibiotic treatment, to improve the effectiveness of antibiotics without an accompanying increase in side effects or sustained effects.[9]

All hospitals in Indonesia, including the Dr. Soetomo General Hospital, are currently preparing an antibiotic stewardship strategy through the establishment of the Antimicrobial Resistance Control Program (ARCP) based on Minister of Health Regulation no. 8 of 2015.[10] The purpose of this research was to determine the bacterial profiles of burn patients, and evaluate the antibiotic therapy administered to them. The data obtained could then be used to refine guidance on antibiotic usage, and support the development of the ARCP at the Dr Soetomo General Hospital.

Materials and methods

This was an observational descriptive study, conducted at the Dr. Soetomo General Hospital in Surabaya. The study used data from the medical records of burn patients treated in the Burn Unit of the hospital between February and May 2018. The data were taken from the patients' medical record, records of drug usage (antibiotics) and culture results (bacterial sensitivity test for antibiotics). The inclusion criteria were patients who were treated in the Burn Unit, were diagnosed with or without comorbidities and did not receive any antibiotics after the burn injury occured. Exclusion criteria were patients who had been diagnosed with combustion but had died before culture swab and/or had received antibiotics after the burn injury occured.

Total antibiotic usage was calculated using the Defined Daily Dose (DDD) method per 100 days. The quality of antibiotic usage was assessed using the Gyssens method.[11] The test results for bacterial sensitivity to antibiotics were divided into 3 groups, namely: sensitive (> 60% bacterial growth was inhibited), intermediate (30-60% bacterial growth was inhibited), and resistant (<30% bacterial growth was inhibited).

Statistical analysis

The profile for antibiotic usage was analyzed by making a summary of usage calculations based on DDD units per 100 days of hospitalization and the Gyssens method. The data were analyzed descriptively using SPSS 17.0.0 for Windows software, 2007, SPSS Inc. Chicago, IL, USA and Microsoft Office 2013.

Ethical clearance

The study received ethical clearance from the Dr. Soetomo General Hospital before it began (Ethical Clearance Number 32/pan.KKE/I/2018). Details that could disclose the identity of the subjects were omitted.

Results

Characteristics of the subjects

There were 21 patients in this study: 16 patients were male and 5 patients were female. Most subjects were in the 26-45 years age group and the smallest number were in the toddlers and elderly groups. Regarding the extent of burns, the majority had a %TBSA (Total Body Surface Area) burned of more than 60%. As for the etiology of burns, 76% were caused by flame and 19% were caused by electricity. As far as clinical outcome was concerned, 9 of the 21 patients died: 5 of them had a %TBSA of more than 60% (*Table I*).

Table I - Characteristics of the study subjects

	n.	%
Gender		
Male	16	76
Female	5	24
Age group		
0-5 years old	1	4.76
6-11 years old	0	0
12-25 years old	2	9.52
26-45 years old	12	57.14
46-65 years old	5	23.8
>65 years old	1	4.76
%TBSA		
≤ 10	3	14.28
10.1 – 20	1	4.76
20.1 – 30	5	23.8
30.1 – 40	1	4.76
40.1 – 50	1	4.76
50.1 – 60	3	14.28
> 60	7	33.33
Etiology		
Flame	16	76
Electric	4	19
Scald	1	5
Outcome		
Recovery	12	57
Death	9	43

Evaluation of antibiotic usage

Eight groups of antibiotics were used for the 21 patients in the Burn Unit at the Dr. Soetomo General Hospital. The most widely used antibiotic was *ceftazidime,* with DDD/100 days of 22.25 (*Table II*). Cultures from 15 of the 21 patients were examined prior to antibiotic administration. Based on the quality

analysis of antibiotic usage using the Gyssens method, it was found that 33.3% were in category 0, and 66.7% were in category IV (*Table III*). Gyssens et al.[11] divided antimicrobial usage into six main categories: appropriate (category 0), inappropriate timing (category I), inappropriate dose and route of administration (category IIa, IIb, IIc), inappropriate duration (category IIIa, IIIb), inappropriate type (IVa, IVb, IVc, IVd), inappropriate indication (category V), and incomplete data (category VI). Based on the antibiotic sensitivity test on the germs in the Burn Unit, amikacin was found to be the most sensitive, compared to the other antibiotics available in the Burn Unit. (*Table IV*).

Table II - DDD/100 days calculation

Type of Antibiotics	n.	DDD/100 days
Ceftazidime injection 1gram	21	22.25
Meropenem injection 1 gram	9	7.54
Ceftriaxone injection 1 gram	6	4.31
Amikacin injection 500 milligram	4	3.59
Cephazolin injection 1 gram	4	1.99
Levofloxacin injection 750 milligram	3	2.42
Fosfomycin injection 1 gram	3	0.03
Cefuroxime injection 750 milligram	1	1.14

Table III - Gyssens method analysis results

Category	Frequency	%
VI (Incomplete data)	0	0
V (Inappropriate indication)	0	0
IV A (There is a more effective alternative)	10	66.7
IV B (There is a less toxic alternative)	0	0
IV C (There is a less costly alternative)	0	0
IV D (There is a narrower alternative)	0	0
III A (Duration is not too long)	0	0
III B (Duration is too short)	0	0
II A (Inappropriate dose)	0	0
II B (Inappropriate interval)	0	0
II C (Inappropriate route)	0	0
I (Inappropriate timing)	0	0
0 (Appropriate)	5	33.3

Table IV - Antibiotic sensitivity in the Burn Unit

Antibiotics	n. sensitive	n. resistant	n. total	%
Amikacin	15	12	27	55.56
Levofloxacin	10	16	26	38.46
Fosfomycin	10	10	20	50
Tetracycline	9	9	18	50
Cefoperazone-sulbactam	8	16	24	33.33
Piperacillin tazobactam	5	18	23	21.74
Meropenem	4	8	12	33.33
Gentamycin	3	25	28	10.71
Tobramycin	1	19	20	5
Ampicillin-sulbactam	1	26	27	3.7
Ceftazidime	1	22	23	4.35
Clindamycin	1	1	2	50
Daptomycin	1	0	1	100
Ciprofloxacin	1	24	25	4
Imipenem	1	8	9	11.11
Ertapenem	0	10	10	0

Bacterial profile

Culture swabs were taken from 15 patients before antibiotic administration: 35% showed negative results. For the 65% of patients with positive bacterial culture, the most common germs were *Bacillus cereus* (12%) and *Acinetobacter baumanni* (12%) (*Table V*).

Table V - Bacterial profile

Type of bacteria	%
Negative results	35
Pseudomonas aeruginosa	11
Enterobacter sp	6
Klebsiella pneumonia	6
Bacillus cereus	12
Acinetobacter baumannii	12
Citrobacter freundii	6
Extended-spectrum beta lactamase +	6
Pseudomonas putida	6

Discussion

With regards to the results of culture prior to antibiotic administration of the 15 burn patients, 35% had no germ growth. This finding showed that the wound surface was sterile after burn injury in some patients. However, some microorganisms would immediately form colonies if proper treatment was not given.[12] Normal flora of skin, airways, and the human digestive tract usually form colonies in the site of wounds, including burn injury wounds. Some aerobic bacteria, such as *Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, Klebsiella spp. and Enterococcus spp* are known to be the main contaminants in burns, besides *Candida spp., Aspergillus*, and *Fusarium* fungi.[13] The most common bacteria found were *Bacillus cereus* and *Acinetobacter baumannii*. A previous study conducted at the DR. M. Djamil Hospital in Padang revealed that the most common bacteria in the burn unit were *Staphylococcus aureus, Klebsiella ozaenae* and *Klebsiella pneumonia.*[14]

Regarding the results on antibiotic sensitivity, this study refers to the Sanford Guide to Antimicrobial Therapy, in which the sensitivity of antibiotics is divided into 3 categories, namely: usually effective clinically, if sensitivity results are more than 60%; clinical trials lacking, if results show sensitivity of between 30-60%; and not effective clinically, if the results are less than 30%. Ac-

cording to the findings of this study, there were no sensitive antibiotics (>60%) for all the germs in the Burn Unit. The highest sensitivity was to amikacin at 55.56% and fosfomycin at 50%.

Germ resistance is created by microorganisms that make enzymes, and these enzymes have the characteristic of destroying drug activity, changing the nature of permeability to the drug, and changing internal structure so that no part is damaged by the drug. Microorganisms change the nature of their metabolism in a way that cannot be inhibited by drugs, and produce enzymes for their metabolism, thus they still exist despite interference from the drug. Resistance occurs due to germs synthesizing enzymes that can turn active substance into inactive, therefore resistance through antibiotics occurs; for example, resistance to the beta lactam group, where penicillin is converted to inactive *penicilloic* acid. Many bacteria, including both gram positive and gram negative, are capable of producing beta lactamase. This enzyme has a large role in causing germ resistance to penicillin. The variety of germs in swab results was due to nosocomial infection. Moreover, length of wound exposure before antibiotic administration is also very influential.

Gyssens flow method was used to evaluate antibiotic usage. Based on our findings, the appropriate use of antibiotics was low. In accordance with the actual protocol, swabs must be performed on every burn patient before antibiotic administration to find out whether the antibiotics that have been given are still sensitive or not. However, limited insurance coverage meant the swab was not carried out, and culture checks were carried out if the patient had signs of sepsis. Proper and rational administration of antibiotics is beneficial for patients, providing maximum results with a low risk of side effects, faster healing, reduced treatment costs and a decrease in antibiotic resistance. The choice of antibiotics available for these patients was the beta-lactam group combined with intravenous anti beta-lactamase or second generation cephalosporin, intravenous generation 3 or intravenous fluoroquinolone respiration. One of the most common antibiotics used for these patients was ceftriaxone, a 3rd generation cephalosporin antibiotic with broad spectrum properties. It has several advantages over other cephalosporin third-generation antibiotics, which are: cheaper, does not require dose adjustment in renal impairment, has a longer half-life, and the risk of allergic reaction is low.

The mechanism of ceftriaxone is to inhibit bacterial cell wall synthesis by binding to one or more penicillin-binding proteins (PBPs), which inhibits the final step of *transpeptidase* from peptidoglycan synthesis in the bacterial cell wall, then inhibits bacterial cell walls. Ceftriaxone is a broad-spectrum antibiotic that is effective against most aerobic bacteria, both gram negative and gram positive, has activity against some gram-negative anaerobic bacteria, and is more active against *enterobacteriaceae* bacteria, including strains that produce beta-lactamase. The DDD value in the prospective period has decreased compared to the retrospective period, which proves that antibiotic usage in the Burn Unit is limited according to indication. The use of appropriate antibiotics plays an important role in preventing resistance.

One of the WHO and CDC recommendations is to implement a program, namely Antibiotics Stewardship, as one of the follow up strategies against antibiotic resistance.[8] The Antibiotic Stewardship Program is an institutional program to enhance the understanding of wise antibiotic usage, a collaboration of various multidisciplinary sciences to raise awareness of how to use antibiotics wisely. In Indonesia, the control of microbial resistance in hospitals has become a government program, listed in Health Minister Regulation No. 8 of 2015. There are 2 strategies for ARCP at hospital.[10] The first strategy is to control the development of resistant microbes by using antibiotics wisely. The second strategy is to prevent the spread of resistant microbes through increased adherence to the principles of infection prevention and control. This program is conducted collaboratively between hospitals, health professionals, communities, pharmaceutical companies and local governments, under the coordination of the Central Government through the Ministry of Health.

Conclusion

Antibiotics are not yet used wisely in the Burn Unit of the Dr. Soetomo General Hospital. Based on the results of culture swabs from burn patients in the hospital's Burn Unit, the most common bacteria in burn patients were *Acinetobacter baumannii* and *Bacillus cereus*.

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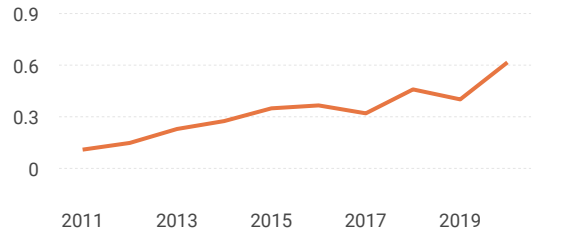

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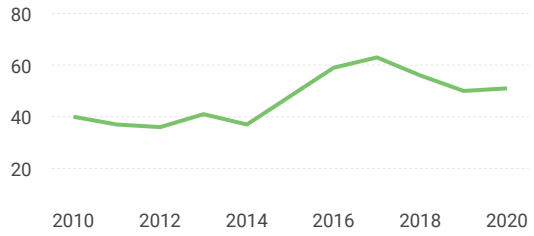

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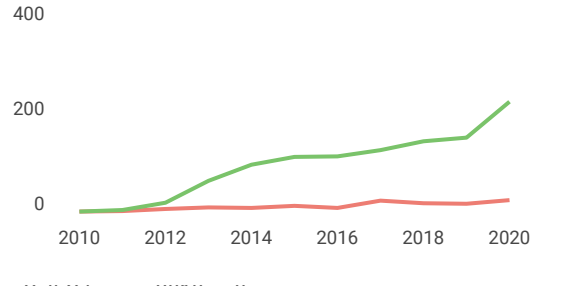

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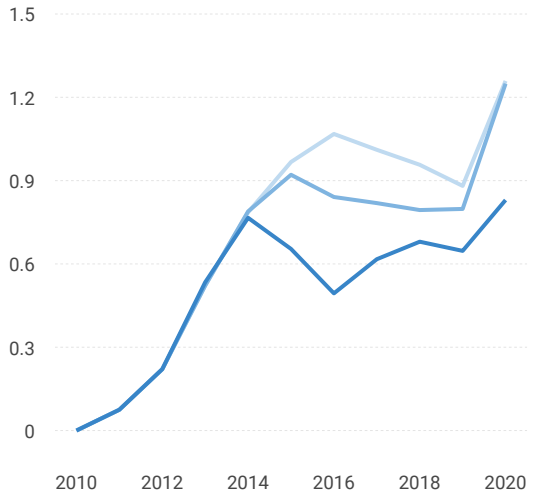

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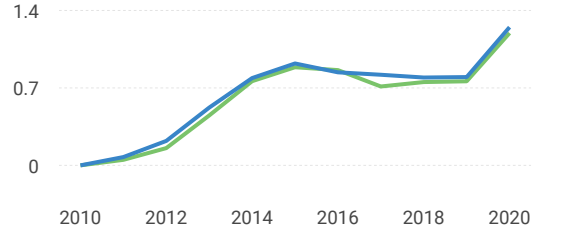

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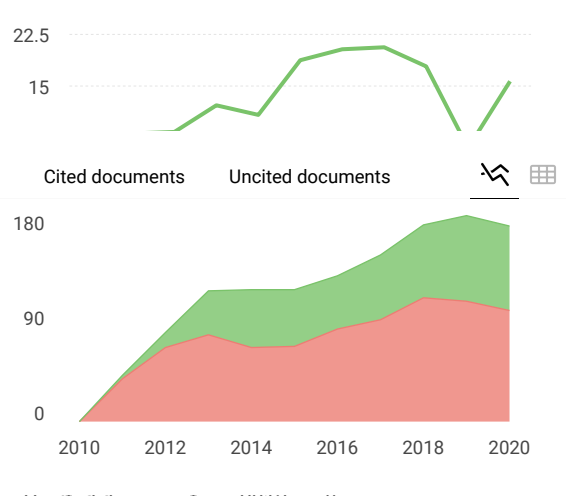

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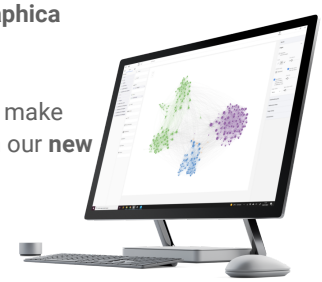

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