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Review Article

A Review of Antibiotic Consumptions at Moewardi Municipality Hospital Dental Ward Surakarta, Indonesia Using Algorithm Gyssens

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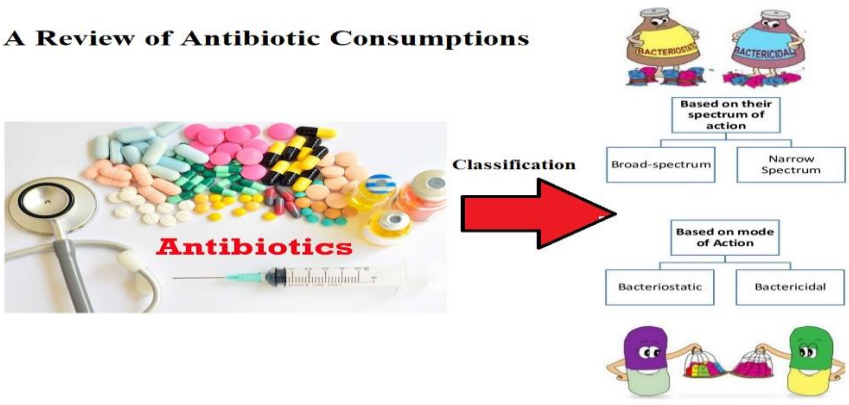
ABSTRACT

Antibiotics are chemicals that kill or stop the growth of microscopic organisms or microbes, such as bacteria, fungi, or protozoa. Therefore, antibiotics can be used to treat diseases caused by germs in the body. The objective of the research was to know the description and pattern of antibiotic prescription at Dr. Moewardi Municipality Hospital Dental Ward, Surakarta. This study was based on the observational description with a cross-sectional study design. The samples taken for observation were 321 patients with medical records from September-December 2018. We applied secondary retrospective data and Defined Daily Doses (DDD)/Anatomical Therapeutic Chemical (ATC) from World Health Organization (WHO) Constanta. The data was then rated for its accuracy by tracing using Algorithm Gyssens. The results showed 71.96% of the patients received treatment and drug prescriptions, of which 36.45% were antibiotics. Amoxicillin was the most widely used antibiotic, followed by Clindamycin and Cefixime. The DDD/ATC ratio was 1.639982. The results from observation and identification with Gyssens category revealed that the categories 0, IIA, IIIB, IIIA, IVB, and V accounted for 75.35%, 2.82%, 8.45%, 7.75%, 4.93%, and 0.7%, respectively, of the consumed antibiotics. Accordingly, there is a rational prescription at Dr. Moewardi Municipality Hospital Dental Ward, Surakarta, but it still needs improvement.

GRAPHICAL ABSTRACT



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Introduction

Antibiotics, often known as antimicrobial medications, are chemicals that kill or limit the development of bacteria in order to treat diseases in humans, animals, and plants. Antibiotic resistance occurs when a bacteria's capacity to kill or its growing is compromised by a specific antibiotic. Antibiotic resistance is a normal phenomenon in some microorganisms [1-5]. A more concerning issue is when bacteria that are typically sensitive to antibiotics develop resistance due to genetic alterations. Antibiotics were discovered more than 75 years ago and have been used by health practitioners as preventive treatment and therapy for suspected microbial infections [6, 7]. However, gradually many microbes have developed resistance against some antibiotics [8–13]. Antimicrobial Resistance (AMR) is the adaptive ability of a microbe with chemical components or drugs that are supposed to terminate or hamper the growth of the microbe. The developed antibiotic resistance by microbes enables them to rapidly proliferate and with unpredictable acquired properties, which may require a wide scope of different antibiotic therapies towards a specific illness or infection [14–17]. According to the World Health Organization (WHO), AMR is currently a global health problem in the treatment of humankind, for instance, Methicillin-resistant Staphylococcus aureus (MRSA) causes more death in the United States every year compared with HIV/AIDS, Parkinson's disease, emphysema and homicide [18, 19].

WHO ratified the global action plan to overcome AMR in May 2015 at the 86th World Health Assembly (WHA) [14]. Consequently, Negara Kesatuan Republik Indonesia (NKRI), as a member of WHO, declared the commitment to participate in the global strategy for controlling antimicrobial resistance [20]. According to Permenkes No. 8 of 2015, the antimicrobial resistance control program is done by rational use of antibiotics and through compliance with the established WHO standards for microbial prevention and infection control [21].

Several studies have been conducted about the rational use of antibiotics in Indonesia. The study about the rational use of antibiotics at Dr. Soetomo Municipality Hospital, Surabaya and Dr. Kariadi Municipality Hospital, Semarang as Teaching Hospital in Indonesia, reported that 30-80% of the drug prescriptions were not in accordance with the medical indication. Consequently, the study reported that only 21% of the drug prescriptions were considered as rational, 15% as improper selection and while 42% was for unnecessary prophylaxis [22]. Another study at the Intensive Care Unit of Dr. Ramelan Navy Hospital, Surabaya, conducted for three months from February-May 2016, showed the calculation result of antibiotic consumption of 151. 63 Dose of Today (DOT)/100 days per patient. The accuracy of antibiotic prescription quality indicated that 52.73% was rational therapy, 8. 18% was irrational, 7.27% was without indication, and 31.82% could not be interpreted by the observer [23].

There are two types of benchmarks that can be used for antibiotic evaluation and consumption quantity calculation. First is the percentage of in-patients on antibiotic treatment during their residence at the hospital, and the second is the quantity of antibiotic consumption with Defined Daily Doses (DDD) per 100 days per patient. Quality appraisal for antibiotic utilization was conducted using the appraisal flowchart developed by Gyssens [20, 24]. The ideal antimicrobial treatment is based on microbial strain compatibility, which is determined through laboratory tests. In addition, the Algorithm Gyssens principle for the use of antibiotics is based on an adaptation to lower the toxicity and thereby reduce the risk of using overpriced drugs, a process called "streamlining." The use of compatible antimicrobials and withdrawal of the non-compatible ones have many advantages. A case in point is the use of the previously successfully used antimicrobials having advantages over the new brands, which lack medical affirmation about their effectiveness. Besides, the Algorithm Gyssens principle also reduces the risk of side effects or adverse events of antibiotics and other drug therapies. The purpose of doing "streamlining" is to measure

and evaluate the effective empirical therapy with precise duration and timing [24].

According to the Law from Ministry of Health Republic Indonesia No.8-year 2015, one of the guidelines for rational antibiotic use is by doing surveillance for the antibiotic usage pattern and reporting it periodically. Several studies of qualitative evaluation for drugs prescription in Indonesia have been done, but fewer studies have addressed the issue at the Dental ward in the hospital or private dental clinics [21].

Research Methodology

This study was an observational descriptive with retrospective data collection and cross-sectional study design. The data was secondary data from medical records of Dental Ward's patient at Dr. Moewardi Municipality Hospital from September-December 2018. Total samples were 321 medical records which contained information on the patient's treatment history and antibiotic use. The data collection method was by total sampling from the whole population who fulfilled the criterion for inclusion into the different Gyssens categories. DDD was computed using the formula below that has been set by WHO:

$$\frac{Utilization\ in\ DDD}{(Sum\ of\ person)\ \times\ (Sum\ of\ days\ in\ the\ data\ collection\ period)} \times 1000 \quad (1)$$

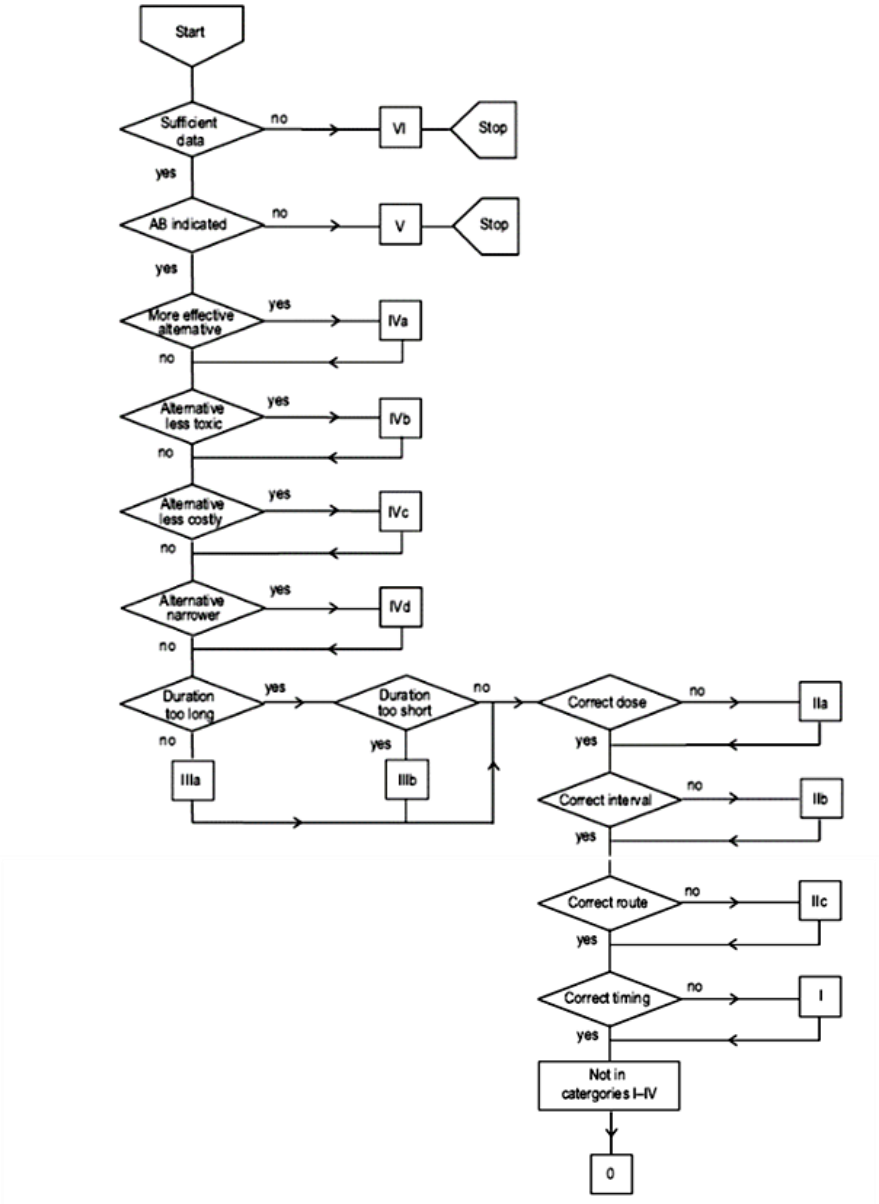

Figure 1: Appraisal flow chart of antibiotic use by Gyssens [16]

Gyssens appraisal flowchart is shown in Figure 1, while the category for the quality assessment of antibiotic use with algorithm Gyssens (see Table 1). Category 0 is the rational use, and Category I-V is irrational to use and prescription, while Category V cannot be evaluated due to lack of information. Data was then processed using Microsoft Excel 2013.

Table 1: Gyssens Appraisal Category

Category	Appraisal
0	Rational antibiotic use
I	Antibiotic use is not on time
IIA	Antibiotic use is improper dose
IIB	Antibiotic use is not in the right interval
IIC	Antibiotic use is not in the right method/route.
IIIA	Prolonged antibiotic use
IIIB	Brief antibiotic use
IVA	There is an alternative antibiotic that is more effective
IVB	There is an alternative antibiotic that is safer
IVC	There is an alternative antibiotic that is more affordable
IVD	There is an alternative antibiotic with a narrower spectrum
V	There is no indication for antibiotic use
VI	The medical record is incomplete and cannot be evaluated.

Results and discussion

In this study, the daily dose per patient and rationality identification was calculated using medical record prescription observation from September-December 2018. Total samples were 321 qualified medical records from 321 Dental Ward patients. The daily dose per patient at the dental ward was determined by using the formula from WHO and ATC guidelines [25]. Assessment of prescription rationality was observed based on several drug use references, including the National Formularium and Drug Prescription for Dentistry Dental Clinical Guidance.

All samples were analyzed based on the Gyssens category as follows: 0 (Rational Antibiotic Use), I (Antibiotic Use is not on time), IIA (Antibiotic Use is improper dose), IIB (Antibiotic Use is not in the right interval), IIC (Antibiotic use is not in the right method/route), IIIA (Prolonged Antibiotic Use), IIIB (Brief Antibiotic Use), IVA (an alternative antibiotic which is more effective), IV B (an alternative antibiotic which is safer), IVC (alternative antibiotic which is more affordable), IVD (an alternative antibiotic with more narrow spectrum), V (no indication for antibiotic use), VI (Medical record is incomplete and cannot be evaluated).

Based on 321 medical records evaluations, we obtained the result for patients' prescription distribution with 231 without prescription (71.96%) and 90 with prescription (28.04%), while the drugs prescription distribution from total samples included 142 antibiotic prescriptions (40.92%) and 205 non-antibiotic prescriptions (59.08%). From the 142-antibiotic prescription, we generated a distribution for antibiotic group and type. The results revealed the top most frequently consumed antibiotic was Amoxicillin, with 59 prescriptions (41.55%). Clindamycin was the second most frequently used antibiotic with 43 prescriptions (30.28%), followed by Cefixime with 33 prescriptions (23.24%) and still other antibiotics with less than 2% prescription such as Metronidazole, Ciprofloxacin, and Tetracyclin.

The highest consumption profile was Amoxicillin with 0.678 DDD/100 dental ward patients per day, while the lowest was Tetracycline 0.00768 DDD/100 dental ward patients per day, while DDD/ATC ratio was computed to be 1.639982 DDD. The results obtained in the current study were slightly lower compared with those of 2013 at Dental Ward University of Kosovo by Haliti et al. (2013), reporting the use of Amoxiclav at 3.12 DDD, followed by Metronidazole at 2.31 DDD, Amoxicillin at 1.25 DDD, and Erythromycin at 0.38 DDD [26]. However, the results from Dental Ward, Dr. Moewardi Municipality Hospital, showed there were still many cases of treatment with first-line antibiotics compared with second-line antibiotics, whereby the latter is considered

as an alternative choice if the first-line antibiotics fail to overcome infection [27, 28]. The results for dose calculation based on the WHO formula are shown in Table 2. Meanwhile, distribution of diagnosis, therapy, and antibiotic prescription with Gyssens Category is shown in Table 3.

Table 2: Calculation of DDD/100 Dental Ward patients per day

Type of Antibiotic	Dose per Tab	Amount of Tablet	DDD/Dental Ward patient per day	DDD
Amoxicillin	500mg	548	0.618538	1.5
	250mg	106	0.059822	
Co Amoxiclav	625mg	3	0.031039	1.5
Clindamycin	300mg	451	0.381179	1.2
Cefixime	200mg	191	0.323378	0.4
	100mg	166	0.140525	
Metronidalzole	500mg	36	0.060951	2
Ciprofloxacin	500mg	10	0.016931	1
Tetracycline	250mg	9	0.007619	1
Total			1.639982	

Table 3: Diagnoses, Therapy, and Antibiotic Prescription with Gyssens Category

ICD 10	Treatment Diagnoses	Antibiotic Group	Frequency	Category					
				0	IIA	IIIB	IIIA	IVB	V
K04.1	Necrosis / Gangrene Pulpa - Extraction	Penicillin	48	47	0	1	0	0	0
		Cephalosporin	0	0	0	0	0	0	0
		Makrolida	15	6	0	2	2	5	0
		Etc	1	0	0	0	0	1	0
K01.1	Impaksi – Odontec-tomy	Penicillin	3	2	0	1	0	0	0
		Cephalosporin	6	4	1	1	0	0	0
		Makrolida	25	17	0	4	4	0	0
		Etc	0	0	0	0	0	0	0
D10. 30	Tumor – OP	Penicillin	0	0	0	0	0	0	0
		Cephalosporin	16	10	1	0	5	0	0
		Makrolida	0	0	0	0	0	0	0
		Etc	0	0	0	0	0	0	0
K11.6	Mucocele - Excision	Penicillin	0	0	0	0	0	0	0
		Cephalosporin	2	2	0	0	0	0	0
		Makrolida	0	0	0	0	0	0	0
		Etc	0	0	0	0	0	0	0
K13. 79	Mouth ulcer - Medication	Penicillin	1	1	0	0	0	0	0
		Cephalosporin	0	0	0	0	0	0	0
		Makrolida	0	0	0	0	0	0	0
		Etc	1	0	0	0	0	1	0
K09.0	Cyst - Enucleate	Penicillin	0	0	0	0	0	0	0
		Cephalosporin	6	3	2	1	0	0	0
		Makrolida	1	1	0	0	0	0	0
		Etc	0	0	0	0	0	0	0
S02	Fraktur Mandibula - Splinting / Medication	Penicillin	0	0	0	0	0	0	0
		Cephalosporin	2	2	0	0	0	0	0
		Makrolida	0	0	0	0	0	0	0
		Etc	0	0	0	0	0	0	0
K05	Gingivitis / Periodon-titis - Medication / Scalling	Penicillin	9	6	0	2	0	0	1
		Cephalosporin	0	0	0	0	0	0	0
		Makrolida	2	2	0	0	0	0	0
		Etc	2	2	0	0	0	0	0
L02. 01	Abses - Drainase / Medication	Penicillin	1	1	0	0	0	0	0
		Cephalosporin	1	1	0	0	0	0	0
		Makrolida	0	0	0	0	0	0	0
		Etc	0	0	0	0	0	0	0
Total			142	107	4	12	11	7	1

Results from Gyssens observation category at Dental Ward, Dr. Moewardi Municipality Hospital was determined to be a prescription with rational use of antibiotic by 75.35% (Category 0) and total irrational use by 24.65% with the breakdown: Improper dose of Antibiotic Use is 2.82% (Category IIA), Prolonged Use of Antibiotic is 7.75% (Category IIIA)), Brief use of Antibiotic w by 8.45% (Category IIIB), 4.93% for an alternative antibiotic which is safer (Category IVB) and 0.7% no indication of antibiotic use (Category V). These results show the rational prescription at Dr. Moewardi Municipality Hospital Dental Ward, Surakarta is higher compared with the same study at Kajen Municipality Hospital, Pekalongan, Middle Java by Saadah in 2015, showing the result of 53.8% antibiotic prescription which falls in Gyssens Category 0 (rational use) and 46.2% in irrational to use [29, 30].

Amoxicillin dominated Gyssens Category 0 with 62 prescriptions. Amoxicillin used for necrose or pulpa gangrene is rational because it is a first-line antibiotic or drug of choice for the dentist. Amoxicillin has spectrum activity that encompasses gram-positive bacteria and gram-negative bacteria but has the lowest toxicity compared with other antibiotics. Spectrum activity in antibiotics is divided between wide spectrum and narrow spectrum in which wide spectrum is for antibiotics that work for two major bacteria groups (gram-positive and gram-negative) while narrow spectrum is for antibiotics that work for certain microbes [27, 31].

Clindamycin irrational prescription makes up nine prescriptions from all. We found there are some of the prescriptions which are irrational because it is not the drug of choice. Clindamycin is a second-line antibiotic agent or alternative choice besides Amoxicillin to cure abscesses and other oral infections. Second-line antibiotics are much more effective but more toxic and have more risk for adverse effects, which is bigger than first-line antibiotics. Spectrum activity from Clindamycin encompasses staphylococcus, streptococcus, and pneumococcus, almost all anaerobe bacteria, including 90% from Bacteroides fragilis, Chlamydia trachomatis, and certain protozoa. Clindamycin is close to antibiotics from the Penicillin group that has an activity for group A and B streptococcus, microaerophilic streptococci, and Streptococcus pneumonia [27, 28, 32]. Low dose Clindamycin use as a medication for post-operation in impaction is correct, which needs multiple omentectomy with full anesthetic. Spectrum activity is widely enough; therefore, the effectiveness is good for targeted bacteria. Some antibiotic has a wide spectrum, including Cephalosporin second and third, Macrolide group, and Amoxicillin with beta-lactam inhibitor or Amoxicillin-clavulanate. Antibiotic and narrow-spectrum do not influence the result of clinical treatment but more to the adverse effect at which the wide spectrum has bigger risk [33].

Cefixime, included in cephalosporin third generation, is widely used for cases that need lots of open wound surgery, for example, Multiple Odontectomy and tumor removal surgery. Antibiotic prescription as prophylaxis therapy aims at preventing infection spread post-operation. The third generation from cephalosporin is used a lot because of the high potential of anti-bacterial and having wide spectrum activity. They are so beneficial for gram-negative infections resistant to penicillin. However, the application of this type of drug also increases the incidence rate of bacterial resistance called β-lactamase–mediated resistance [34].

For the case of gangrene and pulpa necrose, amoxicillin is the recommended first-line antibiotic, but this study found one prescription of Tetracycline. Tetracycline is a wide spectrum antibiotic with wide activity for gram-positive bacteria and gram-negative bacteria, organisms like chlamydiae, mycoplasmas, rickettsiae, and protozoa parasite. Nevertheless, the side effects of Tetracycline use when it is consumed during the permanent teeth development process or eruption process is the greyish area on the teeth surface [35].

Ciprofloxacin (CIP) in this study is prescribed together with Ketoconazole. Therefore, it is included in the Gyssens Category IVB, which

means it is a safer antibiotic. The interaction between Ciprofloxacin dan Ketokonazole hinders the activity of the CYP3A4 enzyme, which has the function to metabolite most drugs, including CIP. This reaction causes a reduction in the effect of Ketokonazole and increases the toxicity of CIP because CIP excretion in the kidney is declining [36].

Two prescriptions of Metronidazole that are considered as antibiotics for anaerobe bacterial in this study are used for Necrotizing Ulcerative Periodontitis (NUP). NUP is a necrose condition as the result of brief onset in the development of periodontic disease. Most bacteria having a relation with the periodontic disease are anaerobe gram-negative bacterial. Several bacteria included in this category are A. actinomycetemcomitans, P. gingivalis, P. intermedia, B. forsythus, C. rectus, E. nodatum, P. micros, S. intermedius, and Treponema sp. [37–39]. Distribution based on the Gyssens's category in this study is summarized in Tables 4 and 5.

Table 4: Antibiotic prescription distribution based on Gyssens's category

Category	Frequency	Percentage
0 – Rational Use	107	75.35%
IIA – Improper Use	4	2.82%
IIIB – Prolonged Use	12	8.45%
IIIA – Brief Use	11	7.75%
IVB – Other safe AB	7	4.93%
V – No AB indication	1	0.7%
Total	142	100%

Table 5: Antibiotic group utilization based on Gyssens category

Antibiotic	Frequency	0	IIA	IIIB	IIIA	IVB	V
Penicillin	62	57	0	4	0	0	1
Cephalosporin	33	22	4	2	5	0	0
Macrolide	43	26	0	6	6	5	0
Etc	4	2	0	0	0	2	0
Total	142	107	4	12	11	7	1

Conclusion

In dental practice, antibiotics are frequently utilized. Antibiotic prescriptions for dental infections are thought to account for 10% of all antibiotic prescriptions. Antibiotic usage in dentistry is characterized by empirical prescription based on clinical and bacteriological epidemiological variables, short-term use of broad-spectrum antibiotics, and the use of a very restricted range of antibiotics. From the review of antibiotic consumption at Dental Ward, Dr. Moewardi Municipality Hospital, we can conclude that most patients have treatment with an antibiotic prescription. However, the DDD for the patient is still in the safe zone with 1.6 DDD. Rational use of antibiotics is 75.5%, while irrational use is 24.5%, and Amoxicillin places the top antibiotic written in the prescription but falls in Category 0 Gyssens. Based on this finding, we can suggest a recommendation to increase the rational use of antibiotics more, especially in the Dental Ward at every hospital with surveillance, appraisal, and periodic report. Other researchers might also do the same study for different health facilities with a certain purpose to control antibiotic use and give a recommendation. Above all, antibiotic stewardship programs and evaluation are still important to be continuously advocated in Surakarta Municipality.

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Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

We have no conflicts of interest to disclose.

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