Original Article

Three years of antibacterial consumption in Indonesian Community Health Centers: The application of anatomical therapeutic chemical/defined daily doses and drug utilization 90% method to monitor antibacterial use

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ABSTRACT

Context: Irrational use of antibacterial drugs in Community Health-Care Centers (CHCs) may lead to increased resistance, morbidity, and mortality. **Aims:** The aim of this study was to determine patterns of antibacterial use at CHCs in a district of Indonesia and use this as data for an antibiotic policy. **Settings and Design:** The observational-descriptive study was conducted in a district of Indonesia to obtain antibacterial use from 2008 to 2010. **Subjects and Methods:** The data obtained from the report on the use of medicines were classified and processed using the anatomical therapeutic chemical (ATC) and defined daily doses (DDD) method, with DDD/1000 patients as a unit measurement. The number of patients was obtained from attending patients in that research period. The most abundant antibacterial drugs use segment was identified by the drug utilization 90% (DU90%) method. **Statistical Analysis Used:** Descriptive analysis were performed in this study. **Results:** Fourteen kinds of antibacterial drugs were used in 61 CHCs. The total of antibacterial drug use during the period 2008–2010 was 871.36 DDD/1000 patients/day. Declining antibacterial use was observed between 2008 and 2010. Six kinds of antibacterial drugs were the most commonly used. The data show that the average use per visit was as high as 24.41 DDD. **Conclusions:** Amoxicillin, sulfamethoxazole and trimethoprim are antibacterials that have to be reconsidered by physicians for use in the Bandung CHC. The high use of antibacterial drugs, as described in the study, can be used as reference to develop an antimicrobial stewardship program and increase awareness of resistance, adverse drug reaction and drug interaction of antibacterial drugs.

Key words: Anatomical therapeutic chemical, antibiotic, defined daily doses, drug utilization 90%, Indonesian Community Health-Care Center, pharmacoepidemiology

INTRODUCTION

Indonesia is a tropical country with a high population density in several locations, which raises the prevalence of infectious diseases. The report from an Indonesian district of health showed that infectious diseases, such as acute respiratory infections, diarrhea, typhoid/paratyphoid, pharyngitis, tonsillitis, bronchitis, chicken pox, and tuberculosis were infectious diseases of high prevalence during the period 2008–2009.[1,2] This led to the inevitable use of antibiotics as anti-infective agents. Problems arise when antimicrobial agents are used irrationally. This irrational drug use may increase morbidity, mortality, incidence of adverse drug reaction, costs, and antimicrobial resistance.[3]

Antibacterial resistance is not simply a local problem but also a serious worldwide concern. The high prevalence of

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antibacterial resistance is caused by many factors, the biggest being the high consumption of antibiotics.[4] Rogues *et al*. also reported the association between antibiotic use and the incidence of antibiotic resistance.[5] Eighty percent of antibiotic agents are being used in the community setting and the remainder in the hospital setting.[6,7] Thus, studies on the use of antibiotics are needed to promote the reduction of the development of antimicrobial resistance, especially in the community setting.[8]

In 1981, The World Health Organization (WHO) recommended the anatomical therapeutic chemical/defined daily doses (ATC/DDD) method as an international standard for drug utilization studies.[9] The method will be used to evaluate the use of medicines and detect an early signal for the irrational use of medicine.[9] The method can be combined with the drug utilization 90% (DU90%) method to identify the high use segment of medicine.

In Indonesia, the Community Health Center (CHC), as the primary health care, is the most visited health-care facility by patients. However, there is a dearth of studies related to the use of medicines, especially antibacterial drugs. Surveillance of antibiotic use is one of the strategies for controlling the use of antibiotics and their resistance.[4,8] The aim of this study was to determine the pattern of antibacterial use in CHC facilities at a district of Indonesia during the period 2008–2010, and possibly let it serve as a database for an antibiotic policy in Indonesian CHC.

SUBJECTS AND METHODS

An observational study was conducted at all CHCs in Bandung City located in an Urban Area of Indonesia. Sixty-one CHCs were observed in relation to their use of antibacterials from January 2008 to December 2010. Data of antibacterial use were extracted from the report on the use of medicines published by the district of health office. These data were processed using the ATC/DDD method.[9] ATC codes and DDD values can be found in the official website of WHO collaborating center for drug utilization study (http://www.whocc.no/atc_ddd_index/).

Data on antibacterials with code ATC J01, were collected and calculated with the unit of DDD/1000 patient/day based on the ATC/DDD guideline.[9] The total amount of every antibacterial drug was converted to gram unit and was calculated by multiplying the total number of antibacterials in each strength by the strength of each antibacterial drug, and the total amount converted to DDD units. The total amount of every antibacterial in DDD units was calculated by dividing the total amount of antibacterial drugs in gram by DDD value of antibacterials as shown on the WHO website. One DDD mean average maintenance dose per day for a drug used is its main indication for adults. More than 1 DDD given to an adult patient per day could be viewed as an indication of an overuse of medicine, and the data used as a signal for irrational use. DDD/1000 patients/years was calculated by dividing the total consumption in 1-year (DDD units) by dividing the total number of visiting patients in the 1-year period with 1000. It can be converted to DDD/1000 patients/day by dividing DDD/1000 patients/years by 365. The figure of 10 DDDs/1000 patients/day amoxicillin (J01CAO4) indicates that 10 out of 1000 patients (or 1%) may have theoretically received a standard dose of amoxicillin (1 g every day).

The number of patients was obtained from the patients attending in the period of study. Patients and pattern of diseases in the place of the study were obtained from the total number of patients attending, and the disease report published by the district health office. Population data were obtained from the census data in 2010, conducted by the National Agency for Statistics giving the growth rates as 1.116% during the period 2000–2010.[10] Data on antibacterial use were analyzed using descriptive statistics, and the most antibacterial use segment identified by DU90% method.[11,12]

RESULTS

The study showed that the patients attending from 2008 to 2010 had increased to a total of 5,178.106. Though there was an increase in the number of patients visiting, there was no increase in the total antibacterial consumption. The total consumption of antibacterial drugs had decreased between 2008 and 2010. However, the ratio of antibacterial drug consumption per visit was 24.41 DDD. The data-related population, patient visits, and antibacterial consumption in this study are shown in Table 1.

Fourteen antibacterial drugs were used in the study period. Most of these were mainly prescribed by the general practictioners in the CHCs, but we found that several in the CHCs were prescribed by a consultant or a nurse. Seven antibacterial drugs were included in the DU90% segment. These were amoxicillin, sulfamethoxazole, trimethoprim, isoniazid, tetracycline, ciprofloxacin, and rifampin. Antibacterial use in the study period can be seen in Figure 1.

There was no significant change in the trend of antibacterial use from 2008 to 2010, but there was a change in the DU90% segment. Rifampicin was not included in DU90% in the year 2009 and 2010, but in 2008 it was included in DU90% segment. The pattern of antibacterial consumption can be seen in Table 2.

Table 1: Population, patient visits, and antibacterial consumption in an Indonesian district during 2008-2010

Information	2008	2009	2010	Total
Population (inhabitant)	2,340,264	2,367,411	2,394,873	7,102,548
Visiting patient (patient)	1,450,082	1,791,128	1,936,896	5,178,106
Antibacterial consumption (DDD)	44,140,088	54,999,406	27,246,363	126,385,858
Ratio of antibacterial use per visiting (total DDD/total patient visit)	30.44	30.71	14.07	24.41
Antibacterial consumption (DDD/1000 patients/day)	367.05	343.21	161.11	871.36

DDD: Defined daily doses

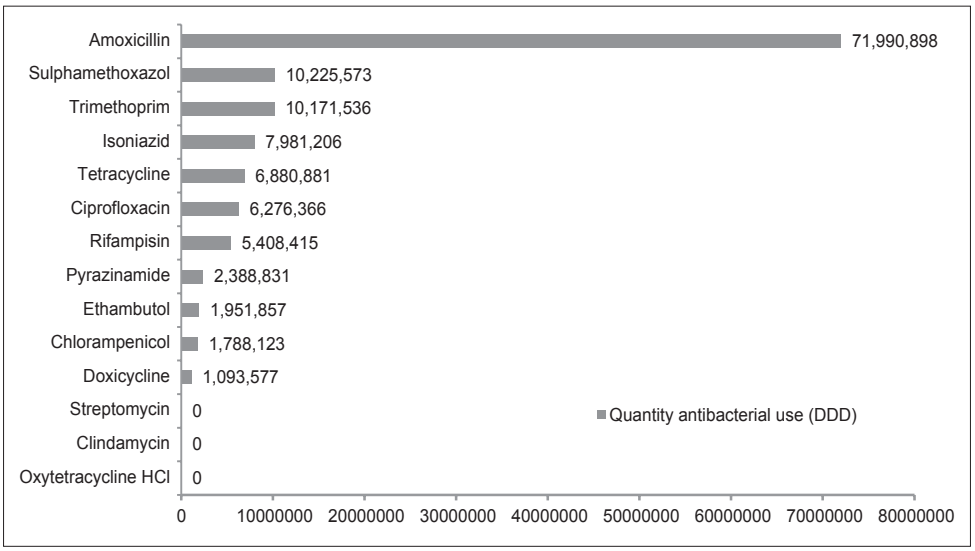

Figure 1: Total consumption of antibacterials in the Community Health Centers in an Indonesian district during 2008–2010 (defined daily doses)

DISCUSSION

In Indonesia, CHC organized by the local government were set up at the sub-district level and coordinated by the district health office. Demographic data in Bandung City showed that population growth rate was 1.116% during the period 2000–2010.[10] The district area was 168.23 km^2, with a population density of 14,236 inhabitants/km^2.[10] There was an increase in patient attendance at the CHCs where the study took place from 2008 to 2010. This could have added to the irrational use of antibiotics.

The data showed that there had been a decline in the use of antibacterial drugs during the period 2008 to 2009 though the ratio of antibacterial consumption per patient visit was still very high. During the study period, patients obtained 24–25 daily doses of antibacterial drugs per visit, which could be a signal for irrational use. Burgess and Abate in 2005 reported 7–10 DDD daily for antibacterial drugs in the outpatients.[13] In our study, though anti-tuberculous drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol) were excluded, antibacterial use per patient visit was 20.95 DDD, which is still very high. Furthermore, the current study population was not limited to patients with infections. There were also those without infections. Thus, the real number of DDD/patient visit would be higher if patients without infections were excluded. In summary, these data indicate an antibacterial overuse for which a strategy for control is required.

There are few important ways of controlling antimicrobial resistance based on the US Center for Disease Control and Prevention. Controlling the use of antibiotic is very important in handling antibiotic resistance. In 1999, Gould reported that antibiotic resistance was affected by the high consumption of antibitoics.[14] Other studies have shown a linear relationship between the incidence of antibiotic resistance and antibiotic consumption.[15,16] Accordingly, the antibacterial drugs included in the DU90% segment are very important for the strict monitoring of resistivity and rationality to prevent the antibacterial drugs from becoming resistant as a result of high consumption. Qualitative studies can be used to follow up the data of DU90% segment to monitor the rational use. In addition, sensitivity and patterns of the use of antibacterials are required for routine monitoring. Monitoring would lead to a shift in the sensitivity pattern of antibacterial drugs and appropriateness of antimicrobial use, Accordingly, there should be local guidance for appropriate selection of antimicrobials. Besides, identification of the DU90% segment can be used as the data to plan the procurement and prediction of adverse events from the most used medicines.

Table 2: Pattern of antibacterial use from 2008 to 2010 in CHCs in an Indonesian district (DDD/1000 patient/day)

Antibacterial	2008	2009	2010
Amoxicillin	202*	200.121*	100.79*
Trimethoprim	31.9884*	26.4148*	9.7528*
Sulfamethoxazole	31.9784*	26.8324*	9.7528*
Isoniazid	23.7183*	16.7021*	8.07442*
Ciprofloxacin	18.4443*	21.7959*	7.9853*
Tetracycline	18.6583*	19.3418*	10.1555*
Rifampin	19.4786*	12.4048	5.97876
Pyrazinamide	6.32132	5.47434	2.40952
Cholamphenicol	5.7578	5.56394	1.34056
Ethambutol	5.10627	4.37637	2.02249
Doxycycline	3.36021	3.78445	1.97668
Streptomycin	0.23303	0.39403	0.3874
Clindamycin	0.000066	0.0016	0.48101
Oxytetracycline HCl	0.00136	0.00176	0.00029
Total	367.047	343.209	161.107

*DU90% segment. CHCs: Community Health Centers; DDD: Defined daily doses; DU90%: Drug utilization 90%

Amoxicillin, trimethoprim, sulfametoxazol, isoniazid, ciprofloxacin, tetracycline and rifampin were antibacterial drugs that were most used in the study period. The high use of these present the greatest opportunity for the development of antibacterial resistance which could then lead to a reduction in the efficacy of antibacterials to the human population. Disease prevalence data indicates that there was a high prevalence of respiratory tract infections, paratyphoid fever, pharyngitis, tonsillitis, varicella, typhoid fever and tuberculosis during the 2008–2009 period. Therefore, a study of antimicrobial resistance is needed to create resistance pattern in the specific area. Resistance patterns can be used to define a second line antibacterial therapy as a basis to develop an antimicrobial stewardship program in the CHC. Furthermore, an evaluation of the appropriate use of antibacterials should be done through a qualitative study to reduce antibaceterial use in the community setting.

The antibacterial overuse shown in this study indicates that some policy is required to improve the situation. Implementation of an antibiotic policy requires knowledge of the limiting factors to a change in antimicrobial prescribing and the effective strategy to improve rational antibiotic prescription.[17] Some factors affecting antimicrobial drug use include: prescriber, patient, facility, and regulation.[18]

Prescriber factor, which is a huge influence in antibiotic prescription, is affected by the prescriber's knowledge, difficulty in diagnosis, patient pressure and financial situation.[18] The condition is worsened by drug promotion by the pharmaceutical companies.[19] In Indonesia, expertise at the CHC such as general physicians, specialist physicians and pharmacists is limited. In some cases, the prescribing is done by other health professionals such as nurses or midwives, which increases the possibility of irrational antibiotic use. The central and local governments have collaborated to increase the number of physicians in the public health facilities. The lack of pharmacy staff can be improved by collaborating with the school of pharmacy in each area to involve pharmacy students (Pharm.D student). Pharmacy students may provide limited pharmaceutical services under supervision, such as drug information, evaluation of antibiotic use, compounding and dispensing of medicine.

Irrational use of antibiotics can be influenced by the knowledge of both healthcare professionals and patients.[20] Several studies have shown inappropriateness of antibiotic needs[21,17] and noncompliance to antibiotic guidelines.[22] Other studies have indicated that patients with little education had misconceptions on antibiotic use.[23-25] Intervention models are required to improve knowledge and awareness of both healthcare professionals and patients. Professional intervention in the effective practice and organization of care group published that several intervention models such as the distribution of educational materials, educational meeting, local consensus processes, educational outreach visits, local opinion leader, patient-mediated intervention, audit and feedback, reminders, marketing, mass media, and financial[26] may be used to change the prescribing behavior in the CHC.

CONCLUSION

The high use of antibacterial drugs described in the study can be used as reference to develop an antimicrobial stewardship program and increase awareness of resistance, adverse drug reactions and drug interaction of antibacterial drugs, especially antibacterial drugs included in the high use segment. Amoxicillin, sulfamethoxazole and trimethoprim are antibacterials whose use in the Bandung CHC have to be reconsidered by physicians. Their use should be closely monitored for any development of resistance and low or diminished efficacy.

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