Erna Kristin et al /J. Pharm. Sci. & Res. Vol. 10(8), 2018, 2065-2068

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Drug Use Pattern in Dengue Patients Who Visited Hospitals and Primary Health Center in Yogyakarta, Indonesia

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Abstract

Studies on the pattern of drug utilization for the treatment of dengue in Indonesia are lacking. The objective of this study was to assess the use of drug treatment for dengue in several hospitals and primary health center (PHC) in Yogyakarta, Indonesia. A retrospective study was conducted on 239 dengue patients in selected hospitals or PHC between April 1st, 2014 and March 31st, 2015. Patients who were clinically diagnosed/laboratory confirmed as dengue with evidence of fever for more than 1 day (plus one of the World Health Organization dengue symptoms) were included. Information on patients' characteristics was gathered from medical records, while drug use data were collected from the prescriptions records. These data were analyzed descriptively. An average of 4.16±2.16 drugs was prescribed per prescription in the hospital, and 2.48±1.21 drugs were prescribed per prescription in PHC. There were 71.6% drugs prescribed in the hospital and 92.7% drugs prescribed in PHC included in the National Formulary. Generics were prescribed in 39.4% and 95.4% drugs in the hospital and PHC, respectively. The most commonly prescribed drugs were analgesics (26.3%), vitamins (14.2%), drugs for acid-related disorders (11.7%), and systemic antibacterials (10.2%). Systemic corticosteroids were prescribed in 6.0% patients. In conclusion, the treatment of dengue patients who visited the hospitals and PHC in Yogyakarta, Indonesia, was rational in some aspects. However, antibiotics and corticosteroids were still used, and positive changes and improvements are needed to increase the rational drug use in dengue patients.

Keywords: dengue, treatment, antibiotic, corticosteroid

INTRODUCTION

Dengue is a viral infection transmitted by Aedes mosquito bite. It is commonly found in the tropics and subtropics, with variations in risk are affected by rainfall, temperature, and urbanization. The global incidence of dengue has increased significantly in recent years. Dengue cases are usually underreported. It is estimated that there are 390 million dengue infections per year (95% CI 284–528 million), with 96 million (67–136 million) cases are clinically apparent [1, 2, 3, 4]. America, South-East Asia, and Western Pacific are the most seriously affected regions [5].

There is no specific treatment for dengue. In severe dengue, the maintenance of body fluid volume is very important. Although the first dengue vaccine has been developed in 2015 and clinical trials are ongoing, currently, the World Health Organization (WHO) recommends prevention by controlling the vector through mosquito habitat removal and insecticide use [6, 7, 8, 9].

According to dengue management algorithm by WHO, patients who suffer from dengue infection are classified into three groups, based on history, physical examination, laboratory results, certain warning signs, and certain concomitant diseases or social conditions. Dengue patients without warning signs can be treated at home, with adequate bed rest, fluid intake, and paracetamol as an antipyretic agent. Dengue patients with certain concomitant diseases or social conditions, or with warning signs should be referred for in-hospital treatment. Patients referred to the hospital due to concomitant disease or social condition reasons are encouraged to take oral fluid, or if the patients cannot tolerate it, they should be given intravenous fluid therapy with 0.9% saline or Ringer lactate at a maintenance rate. Patients referred to the hospital due to warning signs are given an isotonic solution like 0.9% saline or Ringer lactate according to clinical response and hematocrit examination. Patients with severe dengue require emergency treatment. Those who have compensated shock should be given intravenous fluid resuscitation with the isotonic solution until the condition improves. Those who have hypotensive shock should be given intravenous fluid resuscitation with a crystalloid or colloid solution. For those with hemorrhagic complications, fresh packed red cells or fresh whole blood should be given [10, 11, 12, 13, 14].

There has been a lack of studies assessing the pattern of drug utilization for the treatment of dengue in Indonesia. The information on the use of the drug for dengue can provide an insight into the rational dengue treatment in healthcare. This study was conducted with the objective to assess the use of drug treatment for dengue in several hospitals and primary health center (PHC) in Yogyakarta, Indonesia.

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METHODS

This is a retrospective study, conducted on patients who had a diagnosis of dengue or dengue hemorrhagic fever (ICD X code A90 and A91) in selected hospitals or PHC during the period between April 1st, 2014 and March 31st, 2015. The health care facilities in which this study was conducted were a secondary public hospital, private hospital, and PHC of Yogyakarta.

Patients who were clinically diagnosed/laboratory confirmed as dengue cases with recorded evidence of fever of more than 38˚C for more than 1 day (plus one of the World Health Organization/WHO dengue fever symptoms) were included in this study. The medical records of the patients were randomly selected by computer algorithm from a list of all age-stratified dengue diagnoses in the study period. Information on patients' characteristics was gathered from medical records. The drug use data were collected from the prescriptions records for the patients.

Characteristics of the dengue patients were presented in frequency and proportion for categorical characteristics, and in mean ± standard deviation (SD), minimum, and maximum values for continuous characteristics. Drugs were analyzed descriptively on their consistency to the National Formulary and generic drug prescribing. Drugs used for dengue were also classified based on their therapeutic classes, level of healthcare (PHC or hospital), and type of healthcare (inpatients and outpatients).

RESULTS

This study included a total of 239 dengue patients, consisted of 178 (74.5%) hospital patients and 61 (25.5%) PHC patients. The patients were mostly males (54.0%) and they were mostly in the age range of under 12 years old (35.5%) and between 17-25 years old (26.8%). In the hospital, the proportion of males was similar, while in PHC there were more female patients (52.5%). Patients with age range of 17-25 years old were more prominent in the hospital (30.9%), while patients under 12 years old were the most dominant in PHC (55.7%). As expected, most dengue patients

(73.0%) who came to the hospital were later hospitalized, while all who came to the PHC were treated as outpatients. Patients who were hospitalized stayed for an average of 5.50±2.98 days (Table 1).

In the hospital, there was an average of 4.16±2.16 drugs prescribed in a prescription for dengue patients; while there was an average of 2.48±1.21 drugs prescribed in a prescription for dengue patients who visited PHC. The maximum number of drugs prescribed in one prescription was 10 in hospital patients and 7 in PHC patients (Table 1). Compared to drug list in the National Formulary, 71.6% drugs prescribed for dengue patients in the hospital were included in the National Formulary, while there were 92.7% drugs prescribed for dengue in PHC were consistent with the National Formulary. Only 39.4% drugs were prescribed as generics in the hospital, as opposed to 95.4% drugs prescribed as generics in the PHC (Table 2).

Based on therapeutic class, the most commonly prescribed was from the analgesic class (26.3%), followed by vitamins (14.2%), drugs for acid-related disorders (11.7%), and antibacterials for systemic use (10.2%). Aside from antibacterials, non-symptomatic drugs prescribed were systemic corticosteroids (6.0%) (Table 3).

In the hospital, the most prescribed drug was paracetamol (20.1%), followed by multivitamins (10.5%), ranitidine (9.0%), domperidone (6.1%), ondansetron (5.2%), dexamethasone (4.7%), cefixime (4.7%), ceftriaxone (2.8%), and methylprednisolone (2.3%). Drugs prescribed in PHC followed an almost similar pattern, namely, paracetamol (37.7%), pyridoxine (9.9%), ascorbic acid (9.3%), multivitamins (7.3%), ranitidine (4.0%), and domperidone (4.0%). No prescription of antibacterial drugs in PHC, but there were prescriptions of dexamethasone (0.7%) and methylprednisolone (0.7%) (Table 4).

Table 5 shows the drugs used for dengue in inpatients and outpatients. The pattern is similar to the drug use pattern shown in Table 4. In inpatients, paracetamol was the most commonly prescribed (17.2%), followed with multivitamins (11.3%), ranitidine (10.1%), ondansetron (6.1%), dexamethasone (5.6%), domperidone (4.8%), ceftriaxone (3.4%), methylprednisolone (2.7%), and cefixime (2.3%). In outpatients, the most commonly used drugs were paracetamol (36.4%), followed by domperidone (7.7%), cefixime (7.7%), multivitamins (7.0%), pyridoxine (5.5%), and ascorbic acid (5.1%). Dexamethasone and methylprednisolone were prescribed in 0.4% patients each (Table 5).

DISCUSSION

A drug utilization study has been conducted on dengue patients who visited the hospitals and PHC in Yogyakarta, Indonesia. These patients received two to four drugs in a prescription on average. Most of the drugs were in the National Formulary list, but there was a low proportion of generic drug prescribing in the hospital. Analgesics, vitamins, and drugs for acid-related disorders were the most commonly used.

Around 4 drugs on average in a prescription were given for dengue patients in the hospital. Meanwhile, around 2 drugs on average were prescribed for dengue patients who came to PHC. These numbers were better than those reported by another study on drug utilization in dengue patients. A study conducted in a tertiary care hospital in India showed that there was an average of 5 drugs prescribed per prescription for dengue [15, 16, 17, 18]. Another study assessed the drug use only in pediatric patients in a tertiary care hospital in India, in which the average drugs prescribed was 3.8 drugs per prescription [19, 20, 21, 22]. A drug utilization study by Kumar *et al*. showed a smaller average, 2.96 drugs per prescription, but the study was conducted in pediatric outpatients who were generally would be relatively healthier than the hospitalized patients [23, 24, 25, 26]. The high maximum number of drugs prescribed per prescription in our study is quite alarming. The maximum number of drugs prescribed was 10 per prescription in hospital patients and 7 per prescription in PHC patients. The hospitalized patient might have more severe dengue, but all the PHC patients were all treated as outpatients, so the high maximum number per prescription in PHC warrants further investigation.

Table 1. Characteristics Of Dengue Patients

Characteristics	Hospital		PHC		Total	
	n	%	n	%	n	%
Gender						
Male	100	56.2	29	47.5	129	54.0
Female	78	43.8	32	52.5	110	46.0
Age (year)						
0 - 5	25	14.0	21	34.4	46	19.2
6 - 11	26	14.6	13	21.3	39	16.3
12 - 16	27	15.2	7	11.5	34	14.2
17 - 25	55	30.9	9	14.8	64	26.8
26 - 35	18	10.1	5	8.2	23	9.6
36 - 45	12	6.7	5	8.2	17	7.1
46 - 55	13	7.3	1	1.6	14	5.9
> 55	2	1.1	0	0.0	2	0.8
Healthcare						
Inpatient	130	73.0	0	0.0	130	54.4
Outpatient	48	27.0	61	100.0	109	45.6
Length of stay (days)						
Minimum	1					
Maximum	26					
Mean (SD)	5.50 (2.98)					
Prescription						
Minimum number of drugs	1		1			
Maximum number of drugs	10		7			
Mean (SD) number of drugs	4.16 (2.16)		2.48 (1.21)			

Table 2. Characteristics Of Drugs Prescribed For Dengue Patients

	Hospital		PHC	
	n	%	n	%
Consistency with National Formulary list				
Yes	532	71.6	140	92.7
No	211	28.4	11	7.3
Generics				
Yes	293	39.4	144	95.4
No	450	60.6	7	4.6

Table 3. Drugs Prescribed For Dengue Based On Therapeutic Classes

Therapeutic class	n	%
Analgesics	235	26.3
Vitamins	127	14.2
Drugs for acid-related disorders	105	11.7
Antibacterials for systemic use	91	10.2
Drugs for functional gastrointestinal disorders	59	6.6
Corticosteroids for systemic use	54	6.0
Antiemetics and antinauseants	39	4.4
Blood substitutes and perfusion solutions	26	2.9
A cough and cold preparations	23	2.6
Antihistamines for systemic use	21	2.3
Others	114	12.8

The consistency of drugs prescribed to the National Formulary was quite good (71.6% in the hospital and 92.7% in PHC). However, only 39.4% drugs were prescribed as generics in the hospital, while the prescribing of generic drugs was satisfactory (95.4%) in the PHC. Our consistency to the National Formulary was better than that shown by Dutta *et al* study, which reported 62.42% consistency to their National List. They also reported 100% prescription of brand-name drugs for the treatment of dengue [15]. In a study on pediatric patients, there was a better consistency to the National List (91.4%), but a very low generic prescribing (6.3%) [19]. The low number of generic prescribing apparently was common in hospital, as also reported by Kumar *et al*. (20%) [23].

Our study found that the most commonly prescribed drug was analgesics, followed by vitamins, and drugs for acid-related disorders. The fluid therapy was classified into "Others" group, and the proportion was more or less similar with analgesics. When the assessment was conducted further to the name of drugs, paracetamol was the most commonly prescribed for analgesic class, either in the hospital or in the PHC, and also in out- and inpatients. Multivitamins, pyridoxine, and ascorbic acid were the most commonly given vitamins for patients with dengue. Since dengue is a self-limiting viral infection disease, patients are commonly given vitamins to improve their conditions. Other drugs prescribed are symptomatic, for example, drugs for acid-related disorders and antiemetics. This is consistent with the guideline for the treatment of dengue published by WHO [10]. However, there were still prescriptions for antibiotics in dengue patients who visited the hospital. The type of antibiotics prescribed were cefixime (4.7%) and ceftriaxone (2.8%), and some of these antibiotics were given to dengue patients who were treated as outpatients. The inpatients might need antibiotics due to primary or secondary bacterial infection, but the outpatients will be dengue patients who had milder disease who should not receive antibiotics. Further exploration is needed to find out the reasons of antibiotic prescription in these dengue outpatients.

Other studies have documented similar findings on the prescription of antibiotics in dengue patients. In Dutta *et al*. study, 27.52% hospitalized patients were prescribed with antimicrobials, with cefoperazone was the most commonly prescribed, followed by doxycycline and ceftriaxone [15]. In a study on pediatric hospitalized dengue patients, the number was even higher; there were 48.5% antimicrobials were prescribed to these patients [19]. In the dengue outpatients of a tertiary care hospital, 10.6% were prescribed with antibiotics; with ceftriaxone, cefotaxime, and amoxicillin-clavulanic acid were the most commonly prescribed [23]. These findings suggested a common habit of antibiotic drug prescribing in dengue patients, particularly in patients who visited the hospital.

Table 4. Drugs Prescribed For Dengue In The Hospital And PHC

Drug	Hospital		PHC	
	n	%	n	%
Paracetamol	149	20.1	57	37.7
Multivitamins	78	10.5	11	7.3
Ranitidine	67	9.0	6	4.0
Domperidone	45	6.1	6	4.0
Ondansetron	39	5.2	0	0.0
Dexamethasone	35	4.7	1	0.7
Cefixime	35	4.7	0	0.0
Paracetamol, combinations excl. Psycholeptics	26	3.5	1	0.7
Ceftriaxone	21	2.8	0	0.0
Methylprednisolone	17	2.3	1	0.7
Pyridoxine (vit B6)	0	0.0	15	9.9
Electrolytes in combination with other drugs	15	2.0	0	0.0
Ascorbic acid (vit C)	0	0.0	14	9.3
Cetirizine	9	1.2	4	2.6
Carbazochrome	13	1.7	0	0.0
Others	194	26.1	35	23.2

Table 5. Drugs Prescribed For Dengue Based On Type Of Healthcare

Drug	Inpatient		Outpatient	
	n	%	n	%
Paracetamol	107	17.2	99	36.4
Multivitamins	70	11.3	19	7.0
Ranitidine	63	10.1	10	3.7
Domperidone	30	4.8	21	7.7
Ondansetron	38	6.1	1	0.4
Dexamethasone	35	5.6	1	0.4
Cefixime	14	2.3	21	7.7
Paracetamol, combinations excl. Psycholeptics	25	4.0	2	0.7
Ceftriaxone	21	3.4	0	0.0
Methylprednisolone	17	2.7	1	0.4
Pyridoxine (vit B6)	0	0.0	15	5.5
Electrolytes in combination with other drugs	15	2.4	0	0.0
Ascorbic acid (vit C)	0	0.0	14	5.1
Cetirizine	9	1.4	4	1.5
Carbazochrome	13	2.1	0	0.0
Ambroxol	5	0.8	8	2.9
Others	160	25.7	56	20.6

Corticosteroids are sometimes prescribed for more severe dengue, and they are sometimes also prescribed in the earlier stage of dengue with the assumption that they prevent the progression to the more severe stage. However, a recent Cochrane systematic review of 8 studies enrolling 948 patients suggested that the evidence from trials is inconclusive, either for corticosteroids use in more severe or in earlier stage dengue [27, 28, 29, 30]. In our study, we found the use of corticosteroids in dengue patients who visited the hospital and PHC, and in those patients who were treated as inpatients and outpatients. The most commonly used corticosteroid was dexamethasone and methylprednisolone.

Non-rational drug use has several impacts, including a decrease in the quality of drug therapy which may lead to increased morbidity and mortality. There will be a waste of resources due to the use of

unnecessary drugs, which may lead to a decrease in the availability of vital drugs and an increase in treatment cost. Drug adverse effects might occur, and, in the case of non-rational antibiotic use, drug resistance will develop [31]. The results of this drug utilization study on dengue patients give us some insight into the rationality of drug use in these patients. In some elements, drug prescribing for dengue patients was rational, but in other elements, such as in the use of antibiotics and corticosteroids, improvement and change are needed to ensure rational drug use in these types of patients in all levels of healthcare.

CONCLUSION

The treatment of dengue patients who visited the hospitals and primary health centers in Yogyakarta, Indonesia, was rational in some aspects, such as consistency to the National Formulary, generic prescribing, and essential treatment; but in some aspects, positive change and improvement are needed, particularly in the non-rational use of antibiotics and corticosteroids.

ACKNOWLEDGEMENTS

The authors would like to say thank the Director of the Hospitals and Primary Health Centers for sharing their data for this research. Without funding from Center for Health Economics and Policy Studies, University of Indonesia, Jakarta, Indonesia, this research will not be realized. We really appreciated the generosity to give us the funding.

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