Carbapenem and Cephalosporin Antibiotics Usage in Cheras Rehabilitation Hospital

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Abstract

Introduction: Antibiotic resistance is a critical problem faced worldwide. The development of bacterial resistance was often linked to the irrational use of antibiotics.

Objective: This study aimed to describe the prescribing pattern and antibiotics resistance pattern of carbapenems and cephalosporins in Cheras Rehabilitation Hospital (HRC), and to evaluate whether carbapenems and cephalosporins were used in concordance to the National Antibiotic Guideline (NAG) 2008 and 2014.

Methods: This was a retrospective observational study. All adult inpatients treated with carbapenems or cephalosporins from June 2014 to June 2016 were included and the relevant data was extracted from the patients' medical records. The antibiotic prescribing information was compared against the NAG to determine the concordance to the guideline.

Results: There were 64 cases of which carbapenem and cephalosporin antibiotics were prescribed. Majority of the patients (52%) were male with mean age of 46 (standard deviation 18) years old. Ceftazidime was the most prescribed antibiotics (46.9%) followed by Meropenem (17.2%), Cefuroxime (15.6%) and Ceftriaxone (15.6%). The antibiotics were mostly prescribed as definitive treatment (45.3%) while 35.3% and 17.2% of the antibiotics were given as prophylaxis and empirical treatment respectively. Meropenem was the most preferred carbapenems for extended-spectrum β-lactamase (ESBL) infections (35%). ESBL infections were highly sensitive towards carbapenem antibiotics in which the sensitivity rate was 100%. Overall, more than half of the antibiotics (59.4%) were prescribed in concordance to the NAG. Inappropriate indication was the highest non-concordance to NAG found in this study. Eighty percent of Ceftazidime was given as prophylaxis for urodynamic studies (UDS) which was not recommended by the NAG.

Conclusion: This study found that the concordance to the NAG in HRC was satisfactory. Nevertheless, the adherence to the antibiotic prescribing guidelines should be further improved to reduce the emergence of antibiotic resistance.

Keywords: antibiotic usage, carbapenem, cephalosporin

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Introduction

Antibiotics are one of the most common medications prescribed in the hospital. About one-third of hospitalised patients receive antimicrobial therapy (1). It has been shown that beta-lactam antibiotics such as penicillins, cephalosporins, monobactams and carbapenems ranked the highest in antibiotics usage worldwide (2). It also has been reported that a large number of patients receiving antibiotics may be due to inappropriate prescribing behaviour (3).

A study in Ghana reported that antibiotics were the second most commonly prescribed medicines (19.1%) after analgesics (27.1%) (4). Another survey on the utilisation pattern of antibiotics showed that the commonly used classes of antibiotics were Cephalosporins, followed by Fluoroquinolones and Azoles. Although there are standard guidelines on the use of the antibiotics, the differences between the prescribing patterns of antibiotics and the guidelines were still being observed (5).

In Malaysia, only 20% of the antibiotics prescriptions were based on the microbiological test results (6). In the Cheras Rehabilitation Hospital (HRC), Kuala Lumpur, intravenous Cefuroxime and Meropenem were the most prescribed type of antibiotic, by define daily dose (DDD), based on the HRC antibiotic audit done in 2015 (7). The DDD for every 100 admission for these two antibiotics were 15.22 and 22.18 respectively, while DDD for every 1000 patient days was 7.78 and 11.35 respectively. The usage of these antibiotics was higher as compared to other antibiotics that were used in HRC during the period of the study. High antibiotics use may contribute to antibiotic resistance if they are used inappropriately (8). It was proven that bacterial resistance is linked to the bacterial species and the type of antibiotics used (9). Therefore, knowledge about the local antimicrobial resistance patterns of bacteria is a valuable guide to empirical antimicrobial therapy and the formulation of antibiotic guidelines. Ultimately, it is also important for the control of the emergence of antimicrobial resistance in hospitals (10).

This study evaluated the rationale use of carbapenem and cephalosporin antibiotics in HRC. The specific aims of the study were to describe the prescribing pattern and antibiotics resistance pattern of carbapenems and cephalosporins, as well as to evaluate whether carbapenem and cephalosporin antibiotics were used in concordance to the National Antibiotic Guideline (NAG).

Methods

This study was conducted using a retrospective, observational study design with universal sampling method. All adult patients from the adult wards in HRC who was treated with carbapenem or cephalosporin antibiotics during their hospitalisation from June 2014 to June 2016 were included. Patients with incomplete medical records, incomplete of antibiotics course and patients who had started the study antibiotics from other hospital were excluded from the study.

The National Antibiotic Guidelines (NAG) were published to assist prescribers in Malaysia in making decision about the choice of antibiotic treatment (11,12). As NAG 2014 was officially published in December 2014, the antibiotic prescribing information in year 2014 were compared against NAG 2008 and the data in year 2015 and 2016 were compared against NAG 2014.

This study was registered with the National Medical Research Registry (NMRR) and approved by the Medical Research Ethics Committee (MREC) before data collection process was started. The data collection was carried out between October 2016 and February 2017 at the Records Department, HRC. A data collection form was used to record all the relevant data extracted from the patients' medical records. Descriptive analysis which consists of mean, standard deviation and percentage was used to analyse the collected data.

Results

Overall, the mean age of patients in this study was 46 years old (standard deviation 18 years) with a majority of them were males (52%). There were 64 cases of which carbapenem and cephalosporin antibiotics were prescribed. Ceftazidime was the most prescribed cephalosporin antibiotics (46.9%) in the wards followed by Meropenem, Cefuroxime and Ceftriaxone (Table 1).

Urinary tract infection (UTI) was the most common infection (n=31, 48.4%), followed by antimicrobial prophylaxis for urodynamic studies (UDS) (n=24, 37.5%) and pneumonia (n=4, 6.4%). The antibiotics were mostly prescribed as definitive treatment (45.3%) and only 17.2% of the antibiotics were given as empirical treatment (Table 2). Meropenem was the most preferred carbapenem antibiotic for treatment of extended-spectrum β-lactamase (ESBL) infection (n=12, 35.3%) cases detected in the ward.

ESBL infections were highly sensitive towards carbapenem antibiotics in which the sensitivity rate was 100%. For non-ESBL infection, the sensitivity rate towards antibiotic was above 50% except for cefotaxime. Table 3 showed the sensitivity pattern of antibiotics on ESBL and non-ESBL infection detected in HRC.

Table 4 showed the concordance of cephalosporin and carbapenem prescribing to the National Antibiotic Guidelines (NAG) 2008 / 2014. Overall, more than half of the antibiotics (59.4%) were prescribed in concordance to the NAG. Inappropriate indication was the highest non-concordance to NAG found in this study compared to dose, frequency and duration of antibiotic use. Ceftazidime, which was the most prescribed cephalosporin antibiotics, was prescribed for the recommended indication in only 20% of the prescriptions. Eighty percent of Ceftazidime was given as prophylaxis for UDS which was not recommended by the NAG.

Table 1: Cephalosporin and carbapenem usage in HRC (N=64)

Antibiotic	n (%)
Cephalosporin	
Ceftazidime	30 (46.9)
Cefuroxime	10 (15.6)
Ceftriaxone	10 (15.6)
Cefepime	2 (3.1)
Carbapenem	
Meropenem	11 (17.2)
Imipenem + Cilastatin	1 (1.6)

Table 2: Indications of antibiotic usage

Indication	n (%)
Definitive treatment	29 (45.3)
Empirical treatment	11 (17.2)
Prophylaxis	24 (37.5)

Table 3: Sensitivity pattern of antibiotics on ESBL and non-ESBL infection

Antibiotic	Non-ESBL		ESBL	
	Sensitive, n (%)	Resistant, n (%)	Sensitive, n (%)	Resistant, n (%)
Ceftazidime	7 (77.8)	2 (22.2)	0 (0.0)	8 (100.0)
Cefoperazone	10 (90.9)	1 (9.1)	0 (0.0)	11 (100.0)
Cefotaxime	0 (0.0)	1 (100.0)	0 (0.0)	10 (100.0)
Cefuroxime	12 (80.0)	3 (20.0)	0 (0.0)	11 (100.0)
Cefepime	6 (85.7)	1 (14.3)	0 (0.0)	8 (100.0)
Ceftriaxone	1 (100.0)	0 (0.0)	0 (0.0)	1 (100.0)
Imipenem + Cilastatin	1 (50.0)	1 (50.0)	12 (100.0)	0 (0.0)
Ertapenem	1 (100.0)	0 (0.0)	11 (100.0)	0 (0.0)
Meropenem	1 (100.0)	0 (0.0)	11 (100.0)	0 (0.0)

Abbreviation: ESBL - extended-spectrum β-lactamase

Table 4: Concordance of antibiotic prescribing to the NAG 2008 / 2014 *

Category	NAG concordant prescribing, n (%)	NAG discordant prescribing, n (%)
Prescribing information		
Indication (n=64)	38 (59.4)	26 (40.6)
Dose (n=64)	64 (100.0)	0
Frequency (n=64)	61 (95.2)	3 (4.8)
Duration (n=64)	61 (95.2)	3 (4.8)
Antibiotic		
Ceftazidime (n=30)	6 (20)	24 (80)
Cefuroxime (n=10)	10 (100)	0
Ceftriaxone (n=10)	8 (80)	2 (20)
Cefepime (n=2)	2 (100)	0
Meropenem (n=11)	11 (100)	0
Imipenem + Cilastatin (n=1)	1 (100)	0

* Data in year 2014 were compared against NAG 2008 and data in year 2015 and 2016 were compared against NAG 2014.
Abbreviation: NAG - National Antibiotic Guidelines

Discussion

This was a retrospective study on the use of carbapenem and cephalosporin antibiotics from June 2014 to June 2016 in HRC. The result of this study describes the prescribing and resistance patterns of carbapenems and cephalosporins in HRC, and examined whether these antibiotics were used in concordance to the NAC.

During the study period, Ceftazidime was found to be the most prescribed cephalosporin antibiotics. According to NAG 2014, there was an increment in the use of cephalosporins from 2009 to 2013 in all hospitals in Malaysia where it showed increment of 13.25% (12). Malpani *et al*. in her study investigated the utilisation of antibiotics in the hospital and found that cephalosporins were the most commonly used class of antibiotic (5). This showed that broad spectrum antibacterials were more likely to be chosen as the preferred antibiotic among the prescribers. Other considerations that should be acknowledged in antibiotic selections are clinical skills and local sensitivity pattern, adequate knowledge of the pharmacokinetic properties of the antibiotics and factors such as age, allergies and others (13).

Urinary tract infection (UTI) was the most common infection that has been treated with antibiotics in this study, followed by antimicrobial prophylaxis for urodynamic studies (UDS) and pneumonia. This was an opposite trend compared to other studies. For example, a survey by Ali MH *et al*. showed that 41.4% and 28.3% of patients in Newcastle and Edinburgh respectively, were admitted to the ward due to UTI and 78.9% and 48.4% of patients, were admitted due to community acquired pneumonia (14).

ESBL-producing pathogens, particularly *Klebsiella* pneumonia were highly sensitive towards carbapenems in which the sensitivity rate was 100%. However the pathogens were resistant towards all cephalosporins. NAG 2014 showed that a six-year trend (2008 – 2013) of antimicrobial resistant for *Klebsiella pneumoniae* against selective antibiotics in all hospitals in Malaysia was increasing towards the preference of using carbapenem group of antibiotics (12). A clinical update from Paterson and Bonomo stated that carbapenems should be the drug of choice for ESBL-producing organisms as many clinical experienced has been reported before. Some of the published papers showed great use of imipenem compare to meropenem, despite having slightly lower minimum inhibitory concentrations (MICs) as compared to meropenem (15). For non-ESBL infection, except for cefotaxime, the sensitivity rate of carbapenem and cephalosporin antibiotics in HRC was above 50% in our study.

When compared against the NAG, majority of the antibiotics in this study were prescribed according to the guideline. However, Ceftazidime, which was the most prescribed cephalosporin antibiotics, was given as an antimicrobial prophylaxis for UDS in 80% of the cases which was not in concordance to the NAG. There were no new antibiotic recommendations in NAG 2014 as compared to NAG 2008 for UDS (11,12). Although the antibiotic selection for UDS was not in concordance to NAG, these antibiotics had been used in other studies. When using antibiotic prophylaxis in UDS, consideration has to be made whether it benefits the patients in decreasing the post-intervention bacteriuria and other bacterial related complications. A systematic review by Bootsma *et al*. revealed that there was not enough evidence to support the systematic use of antibiotic prophylaxis to prevent UTI in other procedures except for transurethral resection of prostate (TURP) and prostate biopsy (16).

While NAG suggested that antibiotic prophylaxis for urodynamic study is not recommended except in high risk cases, Ceftazidime has been used widely in HRC for UDS. The use of this antibiotic was mainly due to the preference of the clinicians to give antibiotic prophylaxis as negative urinalysis does not eliminate the possibility of post-procedure UTI. Grab M mentioned in his study that for UDS, the antibiotic of choice were fluoroquinolones and trimethoprim-sulphamethoxazole (TMP-SMX) while aminoglycosides, ampicillin and first generation or second generation cephalosporins were the alternatives (17). Another study by Kartal *et al*. showed that the incidence of UTI after UDS was decreased from 14% to 1% when the patients were given prophylaxis dose of ciprofloxacin. There was significant rate of bacteriuria seen after UDS in patients without prophylaxis of ciprofloxacin and the risk factors were identified to be not giving prophylaxis antibiotic before UDS, antibiotic use previously and the presence of pyuria before UDS (18).

Conclusion

This study evaluated the use of carbapenem and cephalosporin antibiotics in HRC. In conclusion, ceftazidime was the most prescribed cephalosporin group of antibiotics in the ward followed by meropenem in carbapenem group. As just slightly more than half of the antibiotics were prescribed in concordance to the NAG, It is recommended to improve physicians' adherence to the national guidelines to reduce the emergence of antibiotic resistance. Collaboration among the doctors, pharmacists, and supporting staffs in programmes such as the Antibiotic Stewardship Program is needed to optimise the use of antibiotics, reduce antibiotic resistance and improve patient outcomes.

Acknowledgement

Conflict of Interest Statement

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