Research Article
Volume 5:2, 2021

Clinical Infectious Diseases: Open Access

ISSN: 2684-4559 Open Access

Evaluation of ceftriaxone use in the medical wards of Universiti Kebangsaan Malaysia Medical Centre (UKMMC) and its outcome

Azlina Ibrahim[1], Isa Naina Mohamed[2], Najma Kori[1], Chee Lan Lau[3], Azmi Mohd Tamil[4], Ramliza Ramli[5], Petrick Periayasamy[1]

[1]Department of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Cheras, Wilayah Kuala Lumpur, Malaysia

[2]Deparment of pharmacology, Universiti Kebangsaan Malaysia Medical Centre, Cheras, Wilayah Kuala Lumpur, Malaysia

[3]Department of pharmacy, Universiti Kebangsaan Malaysia Medical Centre, Cheras, Wilayah Kuala Lumpur, Malaysia

[4]Epidemiology &biostatistics Department of community health, Faculty of medicine University Kebangsaan Malaysia

[5]Department of Medical Microbiology and Immunology, Universiti Kebangsaan Malaysia Medical Centre, Cheras, Wilayah Kuala Lumpur, Malaysia

Abstract

Ceftriaxone is a broad-spectrum antibiotic used to treat or prevent bacterial infections. It has a wide range of gram-negative activity and some gram-positive activity, making it one of the most widely used antibiotics. This study is a prospective study evaluating the use of ceftriaxone in the medical wards. It was the first drug evaluation conducted on ceftriaxone in medical wards of UKMMC. Inpatient records were screened for patients receiving ceftriaxone between August 2018 to December 2018. The appropriateness of ceftriaxone was assessed on the basis of 5 parameters: according to type of therapy (empirical, prophylactic, targeted), indication based on source of infection, total daily dose, dosing frequency, and culture & sensitivity tests. Therapy was deemed appropriate if all 5 criteria were met by the study participants according to local and international antibiotic protocols. Deviation in any of the criteria was considered inappropriate. Patients were followed-up until discharge. Clinical success was considered when there is resolution of signs and symptoms. Clinical failure was considered when there is escalation of antibiotics due to clinical worsening. 325 patients were included. Ceftriaxone use was empirical in 92.9% of patients and one third was indicated for pneumonia (35.4%). The majority of patients were prescribed a total daily dose of 2 g (94.5%) and once daily (96%). Median duration of treatment was 5.0 (IQR 4.0 - 7.0) days. Blood culture and sensitivity test was done in 97.8% of patients. Overall, inappropriate use of ceftriaxone was 55.7%, mostly attributed by inappropriate type of therapy and indication. Factors associated with appropriateness are: concomitant antibiotics, (AOR 2.73, 95% CI (1.55-4.80), P<0.001), length of stay (P<0.023) and duration of therapy (P<0.026).59.7 % of patients had a good clinical outcome, but 13.2% had clinical failure and 1.2% had bacteraemia-related mortality. Inappropriate use of ceftriaxone was high and almost half had no indication to initiate antibiotic. Measures like diagnostic based protocol as antimicrobial stewardship should be implemented to improve the practice of antibiotics.

Keywords: Ceftriaxone • Evaluation • Appropriate • Inappropriate • Medical Wards

Abbreviations: SST: Skin and Soft Tissue; CNS: Central Nervous System; RTI: Respiratory Tract Infection; UTI: Urinary Tract Infection; GIT: Gastrointestinal Infection; CVS: Cardiovascular Infection

Introduction

Ceftriaxone is a broad-spectrum antibiotic used to treat infections that have been proven or strongly suspected to be caused by bacteria. It is a third-generation cephalosporin that inhibits bacterial cell wall synthesis mostly against gram-negative and some gram-positive [1]. It has a high resistance to hydrolysis by many bacterial β- *Llactamases* and also very good tolerability typical of the β- *Lactam* class of antibiotics [2]. Ceftriaxone is one of the most common used antibiotics among antimicrobials due to its wide spectrum of activity, high potency and low risk of toxicity [3]. The reason for its widespread use is its effectiveness in susceptible organisms in urinary tract infections, respiratory tract infections, skin and soft tissue infections, bacteraemia and septicaemia, meningitis, infections in immunosuppressed patients, genital infections and in surgical prophylaxis [3]. However, the global trend shows that this drug has been misused. Research in a specialized hospital in Ethiopia found that the prescribing rate of ceftriaxone was high and primarily used as empiric therapy [4].

A study in Korea concluded that continued empirical use for suspected infection and prophylactic perioperative injection were the reasons for a high degree of improper use of ceftriaxone [3]. Ayinalem et al. cited that most of the inappropriate use of ceftriaxone was seen in terms of duration and dosing frequency, and this is due to low consistency of prescriber to the national standard treatment guideline [5]. This is supported by a study in India that showed a considerably high rate of prescription for cephalosporins and a low rate of policy compliance [6]. Third generation cephalosporins are the most commonly used drugs compared to other generations of cephalosporins, with ceftriaxone being the most widely used cephalosporin [7]. Approximately 10.1% of the annual expenditure on medications for primary care clinics in Malaysia was used for antibiotics in 2011, and approximately 164.97 Million Malaysian Ringgits (MYR) were spent on antibiotics for all Ministry of Health hospitals and primary care clinics in Malaysia [8]. A retrospective study in primary health clinics in Selangor, Malaysia in 2013 showed that health care physicians do not follow the antibiotic guidelines [9]. Antibiotics are often prescribed empirically for all types of infections, including viral infections, and this has led to improper use [10]. Consequently, the misuse of ceftriaxone contributes to the development of antimicrobial resistance and limits the curative power of this drug, leading to higher morbidity and mortality rates and prolonged hospital stays [3].

Globally, studies have shown that resistance to antimicrobial drugs has led to the excessive cost of medical care. Lee et al. argued that antimicrobial drug resistance is projected to add between $100 million and $30 billion annually to health care costs [3]. This is supported by evidence from an Ethiopian study that revealed an annual cost of $4 million to $5 million worldwide for infections caused by antibiotic resistant bacteria due

***Address for Correspondence:** Azlina Ibrahim, Department of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Cheras, Wilayah Kuala Lumpur, Malaysia, Tel: +60142216970, E-mail: azlina1984@yahoo.com*

Received June 05, 2020; **Accepted** February 22, 2021; **Published** March 02, 2021

to improper use of ceftriaxone. Generally antimicrobial drug resistance is largely due to the selective pressure of antimicrobial drug use. Reducing these pressures by prudent administration of these drugs should facilitate the return of susceptible bacteria or, at the very least, prevent or slow down the rate of development of drug-resistant strains. Systemic analysis showed that 4 of the 16 studies provided strong evidence that changes in the prescription of antimicrobial drugs to inpatients could improve the microbial outcome [11]. Despite vigorous efforts to control and promote optimal prescription for antimicrobial use, physicians continue to over-prescribe antibiotics. The improper prescribing of antibiotics may ultimately lead to failure in treatment and pose a threat to patient safety and waste of resources.

Cephalosporin has the highest use among all other antimicrobials in the UKMMC Medical Department from 2010 to 2018, with ceftriaxone being the most prescribed cephalosporin. With this in mind, a prospective study was conducted to evaluate the use of ceftriaxone in UKMMC medical wards. The goal of this study was to evaluate the prescribing pattern of ceftriaxone in UKMMC medical wards and to assess the appropriateness of ceftriaxone on the basis of 5 criteria: indication based on source of infection, type of treatment instituted, total dose per day, frequency of administration per day and presence or absence of blood culture and sensitivity test.

Materials and Methods

A prospective study was conducted to evaluate the use of ceftriaxone by reviewing inpatient medical records between August and December 2018. Patients who received ceftriaxone in medical wards were recruited on the basis of the criterion for inclusion and exclusion. The inclusion criteria were patients older than 13 y of age who had been hospitalized for more than 24 h and who had received at least one dose of ceftriaxone per admission during the study period for the first episode. The exclusion criteria were patients with insufficient information from medical records, patients who were seen in outpatient settings or those who were discharged at their own risk or transferred to another hospital during the course of ceftriaxone. The data collection sheet was filled out based on information from the patient file and/or other medical records. The appropriateness of ceftriaxone was assessed according to the criteria in latest local and international antibiotic protocols. In cases where the criteria are not specified, consultation with an infectious disease physician, a microbiologist, and a senior clinical pharmacist was conducted. Table 1 lists the 5 criteria involved in determining the appropriateness of ceftriaxone in this report.

Patient characteristics were divided into type of wards, age, gender, length of hospital stay and co-morbidity (immunocompromised or non-immunocompromised). The diagnostic criteria for infection in this study are based on the signs and symptoms of a specific infection with 2 out of 4 criteria for Systemic Inflammatory Response Syndrome (SIRS). The four SIRS criteria are fever ≥ 38°C or less than 36°C, abnormal white blood cell (WBC) >12,000 cells/mm3 or <4,000/mm3, heart rate greater than 90 beats per minute, respiratory rate greater than 20 breaths per minute. Therapy was deemed appropriate if all 5 criteria were met by the study participants according to local and international antibiotic protocols. Deviation in any of the criteria was considered inappropriate. All patients were followed up until discharge and clinical outcomes were recorded as clinical success, clinical failure, bacteraemia-related mortality, acquisition of multidrug resistance organisms, and uncertain outcome of ceftriaxone therapy. Uncertain outcome was defined as patients whose outcomes may or may not be related to ceftriaxone therapy. The study involved 325 patients. Statistical analysis was performed using SPSS software version 25. Data analysis includes descriptive statistics and frequency of distribution. Binary logistic regression was performed to determine the association of independent variables with the appropriateness of ceftriaxone and Expressed as Odds Ratios (ORs) with 95% Confidence Intervals (CI). The statistical probability level of $p<0.05$ was considered to be significant. The study was approved by the Medical Research and Ethics Committee of National University of Malaysia.

Results

The data collection sheet of 325 patients was analysed. The median age of participants was 66.0 (IQR 54.5-76.0) years 55.4% were male and 44.6% were female. Table 2 shows baseline characteristics; types of ward, age, gender, length of hospital stay, co-morbidity and SIRS criteria. The median duration of hospital stay was 8.0 (IQR 6.0-12.0) days. Ceftriaxone was prescribed empirically in 92.9% of patients. 76% of patients met SIRS criteria with signs and symptoms of specific infections, while the remaining 24% did not meet SIRS criteria, had no signs and symptoms of specific infections, and therefore, ceftriaxone was not indicated. Among patients who met SIRS criteria with signs and symptoms of specific infection, 23.5% of these patients were not recommended for ceftriaxone based on current evidence guidelines. The most common indication for ceftriaxone was pneumonia (35.4%) followed by 15.4% for sepsis and 12 % for gastrointestinal infections. The most commonly prescribed dose was 2 grams (g) once daily. The median duration of ceftriaxone was 5.0 (IQR 4.0-

Table 1. Five individual criteria involved in the evaluation of ceftriaxone appropriateness.

Criteria	
Type of treatment	Empiric
	Specific
	Prophylactic
Source of infection	Skin and soft tissue infection
	Central nervous system infection
	Respiratory tract infection
	Urinary tract infection
	Gastrointestinal infection
	Cardiovascular infection
	Sepsis
	No indication
Total dose per day(g)	1 gr to 4 gr daily
Frequency of administration per day	Once daily or twice daily
Blood culture and sensitivity test	Absence of presence

Table 2. Baseline characteristics of study participants (N=325).

Criteria		N	(%)
Ward	Medical 5	66	20.3
	Medical 2	58	17.8
	Medical 7	57	17.5
	Medical 1	55	17
	Medical 6	55	16.9
	Acute Admission Unit	15	4.6
	Medical 3	10	3.1
	High dependency ward	7	2.2
	Coronary care unit	1	0.3
	Cardiac rehabilitation ward	1	0.3
Age (median years, IQR)	66.0 (IQR 54.5-76.0)		
Gender	Male	180	55.4
	Female	145	44.6
Length of hospital stay (median days, IQR)	8.0 (IQR 6.0-12.0)		
Co-morbidities	Non- immunocompromised	292	89.8
	Immunocompromised	33	10.2
SIRS criteria	Yes	247	76
	No	78	24

Abbreviations: IQR: Interquartile Range; N: Frequency; SIRS: Systemic Inflammatory Response Syndrome

7.0) days.97.8% of patients had a blood culture and a sensitivity test with only 11.6% of these tests resulted in positive growth. Approximately 20.9% of patients had concomitant antibiotics and the most frequent concomitant antibiotic was azithromycin. (Tables 2 & 3). Of the 325 patients in the study sample, 44.3% received ceftriaxone appropriately in all 5 evaluated criteria, while 55.7% of ceftriaxone prescription was inappropriate (Figure 1). The inappropriate use of ceftriaxone was largely due to incorrect type of treatment and indications (Figure 2). Ceftriaxone was inappropriately prescribed in cases of sepsis followed by urinary tract infection and infection of the skin and soft tissues (Figure 3). 57.3 % patients had no indication of any antibiotic because they had neither SIRS criteria nor any specific signs and symptoms suggesting an infection. Examples of cases with no indication of ceftriaxone in this study were non-infective exacerbations of bronchial asthma, asymptomatic bacteria, viral fever, dengue fever, and cholelithiasis. The dose and frequency of ceftriaxone were not appropriate in 22.2% and 1.1% of patients, respectively (Table 4).

Clinical improvement was seen in more than half of the total study patients (59.7%), compared to 13.2% of them who experienced clinical failure. 1.8% of patients acquired multidrug resistance organisms during hospitalization, while 1.2% developed bacteraemia related mortality (Figure 4).

Table IV shows other factors associated with the appropriateness of the use of ceftriaxone. The results showed that duration of hospital stay, duration of therapy and concomitant antibiotics were significantly

Table 3. Prescription pattern of ceftriaxone in the study participants (N=325).

Criteria		N	(%)
Type of treatment	Empiric	302	92.9
	Specific	15	4.6
	Prophylactic	8	2.5
Source of infection	Respiratory tract infection	115	35.4
	No indication	78	24
	Sepsis	50	15.4
	Gastrointestinal infection	39	12
	Urinary tract infection	28	8.6
	Central nervous infection	12	3.7
	Skin, soft tissue and bone infection	2	0.6
	Cardiovascular infection	1	0.3
Total dose per day(g)	1g	2	0.6
	2g	307	94.5
	3g	3	0.9
	4g	13	4
Frequency of administration per day	OD	312	96
	BD	13	4
Blood culture and sensitivity test	Presence	318	97.8
	Absence	7	2.2
Positive growth	Yes	37	11.6
	No	281	88.4
Duration of therapy (median days, IQR)	5.0 (IQR 4.0-7.0)		
Concomitant antibiotic	Yes	68	20.9
	No	257	79.1
Concomitant antibiotic list (Yes, N=68)	Azithromycin	53	78
	Akurit	5	7.3
	Metronidazole	3	4.4
	Acyclovir	3	4.4
	Cloxacillin	2	2.9
	Erythromycin	1	1.5
	Bactrim	1	1.5

Abbreviations: IQR: Interquartile Range; N: Frequency; OD: Once Daily; BD: Twice Daily; g: Grams

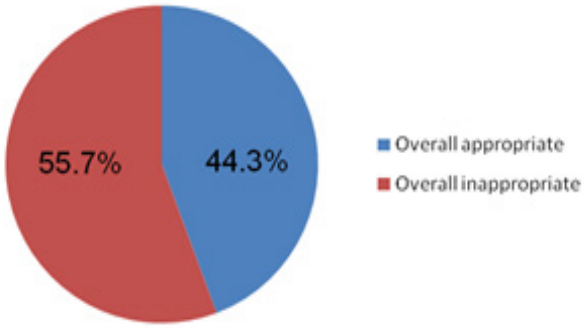

Figure 1. Appropriateness of the use of ceftriaxone in the total study participants (N=325).

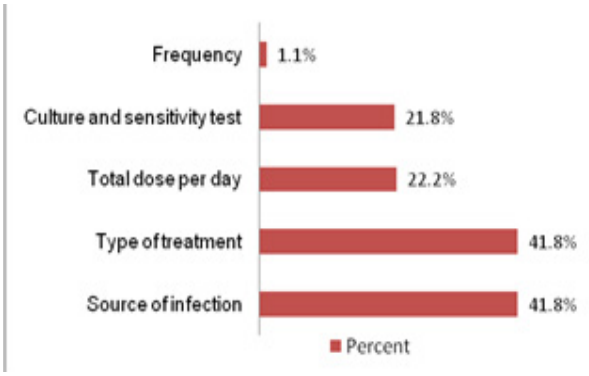

Figure 2. Inappropriate use of ceftriaxone based on 5 test parameters (N = 181).

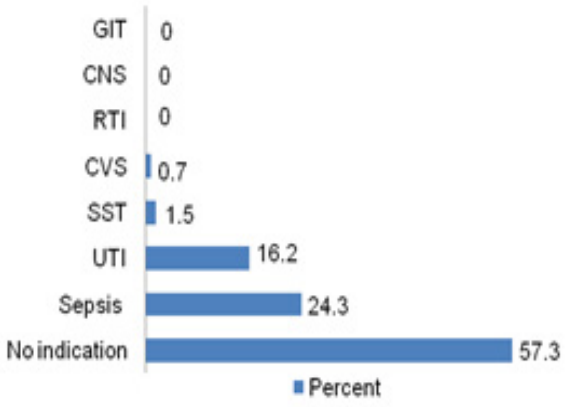

Figure 3. Inappropriate use of ceftriaxone based on the source of infection (N=136).

associated with appropriateness of ceftriaxone use. Other variables such as type of ward, gender of patients, co-morbidities and age of patients have not been associated with appropriateness of ceftriaxone use. In the binary logistic model (Table 5), patients with concomitant antibiotics were more likely to be prescribed ceftriaxone appropriately. The odds ratio of appropriate ceftriaxone therapy was approximately 3 times higher for patients with concomitant antibiotics (adjusted odds ratio 2.7, $p<0.001$) compared to patients without concomitant antibiotics. Patients with shorter duration of hospital stay and shorter duration of therapy were more likely to be prescribed ceftriaxone inappropriately.

Discussion

This study was designed to evaluate the appropriateness of ceftriaxone utilization in medical ward of Universiti Kebangsaan Medical Centre. The current study showed a high level of inappropriate use of ceftriaxone.

Table 4. Factors associated with the use of ceftriaxone in participants (N=325).

Criteria	Appropriate N = 144(%)	Inappropriate N = 181 (%)	χ	P value
Ward, N (%)				
Medical 5	29(43.9)	37(56.1)	16.1	0.064
Medical 2	32(55.2)	26(44.8)		
Medical 7	22(38.6)	35(61.4)		
Medical 1	23(41.8)	32(58.2)		
Medical 6	29(52.7)	26(47.3)		
Acute Admission Unit	3(20)	12(80)		
Medical 3	1(10)	9(90)		
High dependency ward	4(57.1)	3(42.9)		
Coronary care unit	0(0)	1(100)		
Cardiac rehabilitation ward	1(1)	0(0)		
Age (median years, IQR)	67.0 (IQR 52.0-76.0)	65.0 (IQR 54.5-75.0)		0.526 μ
Gender, N (%)				
Male	87(48.3)	93(51.7)	2.65	0.104
Female	57(39.3)	88(60.7)		
Length of hospital stay (median days, IQR)	9.0 (IQR 6.0-13.8)	7.0 (IQR 5.0-11.0)		0.001 μ
Co-morbidities, N (%)				
Immunocompromised	12(36.4)	21(63.6)	0.94	0.332
Non immunocompromised	132(45.2)	160(54.8)		
Based on type of treatment instituted, N (%)				
Empiric	138(45.7)	164(54.3)	9.96	0.008*
Specific	6(40)	9(60)		
Prophylactic	0(0)	8(100)		
Based on source of infection, N (%)				
Respiratory tract infection	112(97.4)	3(2.6)	303.98	0.001*
No indication	0(0)	78(100)		
Sepsis	12(24)	38(76)		
Gastrointestinal infection	6(15.4)	33(84.6)		
Urinary tract infection	3(10.7)	25(89.3)		
Skin, soft tissue and bone infection	0(0)	2(100)		
Central nervous infection	11(91.7)	1(8.3)		
Cardiovascular infection	0 (0)	1(100)		
Total dose per day (g), N (%)				
1g	1(50)	1(50)	12.84	0.005*
2g	132 (43)	175(57)		
3g	0 (0)	3(100)		
4g	11(84.6)	2(15.4)		
Frequency of administration per day, N (%)				
OD	133(42.6)	179(57.4)	7.3	0.007*
BD	11(84.6)	2(15.4)		
Blood culture and sensitivity test, N (%)				
Done	144(45.3)	174(54.7)	5.69	0.017*
Not Done	0 (0)	7(100)		
Concomitant antibiotic, N (%)				
Yes	43(63.2)	25(36.8)	12.49	0.001*
No	101(39.3)	156(60.7)		
Duration of therapy (median days, IQR)	6.0 (IQR 4.0-7.0)	5.0 (IQR 3.0-7.0)		0.004 μ

Abbreviations: N: Frequency; OD: Once Daily; BD: Twice Daily; μ Mann-Whitney U, $\chi 2$ =Pearson Chi Square; IQR: Interquartile Range; P value < 0.05 = Statistically Significant.

Table 5. Factors associated with appropriateness of ceftriaxone usage using binary logistic regression (N = 325).

Criteria	Appropriate	Inappropriate	AOR (95%CI)	P Value
	N =144(%)	N=181(%)		
Concomitant antibiotic (yes)	43 (29.9)	25 (13.8)	2.73 (1.55-4.80)	0.001*
	101 (70.1)	156 (86.2)	1	
Length of hospital stay (median days, IQR)	9.0 (IQR 6.0-13.8)	7.0 (IQR 5.0-11.0)		0.023*
Duration of therapy (median days, IQR)	6.0 (IQR 4.0-7.0)	5.0 (IQR 3.0-7.0)		0.026*

Abbreviations: N: Frequency; AOR: Adjusted Odds Ratio; CI: Confidence Interval; IQR: Interquartile Range; P value<0.05 =Statistically Significant.

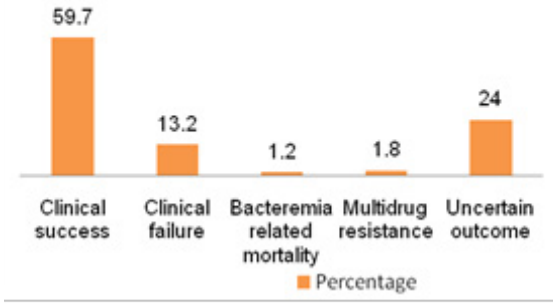

Figure 4. Clinical outcome of study participants (N=325).

Ceftriaxone was prescribed as an empirical antibiotic in 92.9% of the cases in this study. This is comparable to the study conducted at Ethiopians and Port Spain tertiary hospital, where ceftriaxone use was 87.3%, 79.5% and 68% respectively [12-14]. The difference in the degree of ceftriaxone use may be due to the easy availability of ceftriaxone, and clinicians' preferences for a single daily dose and broad spectrum coverage of ceftriaxone against the most common aerobic gram-positive and gram-negative pathogens, local epidemiology and disease spectrum seen here. Lee et al. cited that the common reason for high empirical use of ceftriaxone was its use as an empirical therapy for presumed infections [3].

Ceftriaxone was commonly used in cases of pneumonia (35.4%) followed by sepsis (15.4%) and gastrointestinal infection (12%) in this study. Ceftriaxone was not indicated in 24% of patients who did not meet SIRS criteria or show signs and symptoms of specific infections. The results were similar to the ceftriaxone study in Ethiopia, showing that 35.4% study participants had community-acquired pneumonia and, overall, about 18.5% of participants did not need ceftriaxone in their study [12]. In contrast, two other studies in Ethiopia found that ceftriaxone was most commonly used in gastrointestinal cases (perioperative and abdominal prophylaxis) followed by pneumonia. Variations in the use of ceftriaxone in these studies may be due to the inclusion of surgical patients compared to our research in

which only patients from medical wards participated in the study. The use of ceftriaxone for prophylaxis purposes was only 2.5% (8 cases) in our study, but only 25% was appropriate for prophylaxis use. The reason for ceftriaxone prophylaxis in this study was in patients with gastrointestinal bleeding cirrhosis. Hospital National Antimicrobial Prescribing Survey of ceftriaxone use in Australian Hospital showed that the most common indication for ceftriaxone was community-acquired pneumonia [15-17]. Ceftriaxone use for surgical prophylaxis and infective exacerbation of COPD appears to have a large proportion of inappropriate use [17].

The most commonly prescribed daily dose of ceftriaxone was 2 g in this study (94.5%).This finding was comparable to the study in Ethiopia and Korean Hospitals where the most common daily dosage of ceftriaxone was 2 g in 88.9% and 85.3% [12,3]. Almost 96% of patients received ceftriaxone once daily. Our results differ from the study in Tikur Anbessa Hospital, where the frequency of ceftriaxone administration was inappropriate with 98.4% of their patients receiving ceftriaxone twice a day, and the reason for this was more a tradition of practice [12]. The normal recommended dose of ceftriaxone was once daily, but a review on the pharmacokinetic profile of the normal recommended dose of ceftriaxone in critically ill patients showed that once daily ceftriaxone administration may result in insufficient plasma concentrations in patients with normal renal function who were severely ill with sepsis [18]. Blood culture and sensitivity were reported in 97.8% of cases, but only 11.6% had positive growth. The rate of culture and sensitivity performance in our study was very high compared to the Ethiopian studies, where most of their patients did not have a blood culture and sensitivity test performed despite being on ceftriaxone [12, 16]. Study in Korea suggested a lack of culture and sensitivity test prior to initiation of ceftriaxone, resulting in prolonged continued empiric therapy for suspected infections [3]. The high number of culture and sensitivity tests in our study showed that UKMMC clinicians are well aware of the importance of sending a blood culture and sensitivity test prior to antibiotic delivery.

The top antibiotic combination administered to patients in this study was ceftriaxone and azithromycin in pneumonia followed by a combination of ceftriaxone and Akurit in pulmonary tuberculosis. The outcome analysis showed a relatively high clinical success rate of 59.7%, with only 13.2% of clinical failure following the use of ceftriaxone. Most of the other studies did not evaluate the outcome of the use of ceftriaxone, except for a study in Korea that showed clinical success in 60.7% of cases [3]. These suggest that ceftriaxone has reasonable clinical outcomes when used empirically, but microbiological evidence must be collected prior to initiation of therapy to allow for the detection and testing of specific organisms. Overall, 24% of the total study participants had no indication of ceftriaxone because they did not meet the SIRS criteria had any signs and symptoms suggesting infection. These unnecessary prescriptions are deemed to be a waste of hospital resources and may contribute to the excessive cost of medical care. The rate of multidrug resistance in this study was only 1.8%. This may be due to the short duration of ceftriaxone therapy [median duration 5.0 (IQR 4.0-7.0)] days in our hospital. Literature has shown that the number of days of antimicrobial therapy correlates to the prevalence of resistance [19].

The overall inappropriate use of ceftriaxone was found to be 55.7% in this study. This finding is much lower compared to the other two prospective studies in Ethiopia, where the inappropriate use of ceftriaxone was 87.9% and 80.2% respectively, and the reason for this was the inappropriate duration of therapy [12,13]. A study of ceftriaxone use in Australian Hospital suggested that 30.5% of ceftriaxone use was considered inappropriate and 33.5% was not consistent with any local or national guidelines [17]. The reasons for inappropriate use of ceftriaxone were: failure to use narrow-spectrum antimicrobials, lack of indication and incorrect dose or frequency [17]. In addition, incorrect use of ceftriaxone has been observed in 34.5% of cases in the Korean study, and common reasons for this include continued empiric use for suspected infections, prophylactic perioperative injection, and empiric fever therapy. The most common reason for improper use of ceftriaxone in our study was an inappropriate indication and type of treatment instituted. This could be due to the practice of giving empiric antibiotics for fever despite no clinical, biochemical, radiological or microbiological evidence of bacterial infection. Most patients may have viral illnesses only and therefore the use of empiric antimicrobials in these cases has resulted in additional medical care costs and increased financial burdens in our hospital.

Other factors that have been significantly associated with the appropriateness of ceftriaxone use in this study include concomitant antibiotics, duration of ceftriaxone therapy and duration of hospital stay. The use of concomitant antibiotics contributed significantly to the overall treatment of patients in this study. This is likely due to the fact that physicians are aware of the antibiotic guidelines, for example, the most common concomitant antibiotic used was Azithromycin, seen primarily in community-acquired pneumonia. These results were comparable to those of the study in Gondar Hospital [10]. Ceftriaxone was more likely to be given inappropriately in patients with shorter hospital stays and shorter duration of therapy. This is due to the inappropriate initiation of ceftriaxone in non-indicated cases. As a result, physicians may have agreed to stop the antibiotic earlier, leading to shorter hospital stays and shorter duration of treatment in the overall inappropriately treated patients.

Limitations

There are few limitations to this study. The current study focuses only on medical wards and a more generalized outcome would be achieved if other departments, such as orthopaedic or surgical wards, were included. The duration of ceftriaxone was not included as one of the criteria for assessing appropriateness in this study. No local prospective studies were conducted on the use of ceftriaxone and therefore no local comparison was possible. Therefore, we suggest that this study be performed in another local hospital for comparison in a local setting.

Conclusion

In summary, the study showed a high level of improper use of ceftriaxone in UKMMC medical wards. This unnecessary prescription may cause hospital resources to be wasted and may contribute to the excessive cost of medical care in hospital. We recommend the implementation of a diagnostic based protocol on the use of antibiotics as an antimicrobial stewardship strategy, as the root cause of improper use of ceftriaxone in this study was an inappropriate indication and more than 50% of those who had no infection received ceftriaxone. The diagnostic-based protocol may therefore be a guideline for prescribers to be more selective in the prescription of antibiotics and to reserve antibiotics for cases that have been proven or strongly suspected to have been infected. Prescribers should follow guidelines to prevent unnecessary prescription for more cost-effective treatment.

References

1. Clinical and Laboratory Standards Institute (CLSI).“Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard. Tenth Edition.” USA, 2015.

2. Craig WA. “Pharmacokinetic/pharmacodynamic parameters: rationale for antibacterial dosing of mice and men.” *Clin Infect Dis* 26(1998):1-12.

3. Lee, Hyuck, Dongsik Jung, Joon Sup Yeom and Jun Seong Son, et al. “Evaluation of ceftriaxone utilization at multicenter study.” *Korean J Intern Med* 24(2009):374-380.

4. Sileshi, Alemayehu, Admasu Tenna, Mamo Feyissa and Workineh Shibeshi, et al. “Evaluation of ceftriaxone utilization in medical and emergency wards of Tikur Anbessa specialized hospital: a prospective cross-sectional study.” *BMC Pharmacol Toxicol* 17(2016):7.

5. Ayinalem, Getasew A, Belayneh K. Gelaw, Abebe Z. Belay and Jimma L. Linjesa, et al.“Drug use evaluation of ceftriaxone in medical ward

of Dessie Referral Hospital, North East Ethiopia. *Int J Basic Clin Pharmacol 2*(2017):711-717.

6. John, Shinu Mary, Bijoy Kumar Panda, Deepak Govind Bhosle and Nikki Soman, et al. "Evaluation of cephalosporins utilization and compliance with reference to the hospital antibiotic policy of an Indian tertiary care hospital." *Int J Basic Clin Pharmacol* 8(2019):1044-1050.
7. Gururaja, MP, Sarah A, Samaga L and Joshi H, et al. "Cephalosporin utilization evaluation in a University teaching hospital: a prospective study". *J Drug DelTher* 3(2013):83-87.
8. Alabid, Alamin Hassan MA, Mohamed Izham Mohamed Ibrahim and Mohamed Azmi Hassali. "Antibiotics Dispensing for URTIs by Community Pharmacists (CPs) and General Medical Practitioners in Penang, Malaysia: A Comparative Study using Simulated Patients (SPs)". J *Clin Diagn Res* 8(2014):119-123.
9. Shamsuddin, Shafinaz, Muhammad Eid Akkawi, Syed Tabish Razi Zaidi and Long Chiau Ming, et al. "Antimicrobial drug use in primary healthcare clinics: a retrospective evaluation". Int J Infect Dis 52(2016);16-22.
10. Ayele, Asnakew Achaw, Begashaw Melaku Gebresillassie, Daniel Asfaw Erku and EyobAlemayehu Gebreyohannes, et al. "Prospective evaluation of Ceftriaxone use in medical and emergency wards of Gondar university referral hospital, Ethiopia." *Pharmacol Res Perspect* 6(2018).
11. Davey, Peter, Erwin Brown, Lynda Fenelon and Roger Finch, et al. "Systematic review of antimicrobial drug prescribing in hospitals". *Emerg Infect Dis*12(2006):211-216.
12. Sileshi, Alemayehu, Admasu Tenna, Mamo Feyissa and Workineh Shibeshi, et al. "Evaluation of ceftriaxone utilization in medical and emergency wards of Tikur Anbessa specialized hospital: a prospective cross-sectional study". *BMC Pharmacol Toxicol* 17(2016):7.
13. Ayele, AsnakewAchaw, Begashaw Melaku Gebresillassie, Daniel AsfawErku and EyobAlemayehuGebreyohannes, et al. "Prospective evaluation of Ceftriaxone use in medical and emergency wards of Gondar university referral hospital, Ethiopia". *Pharmacol Res Perspect* 6(2018):e00383.
14. Pereira, Lexley M Pinto, Marjorie Phillips, Hema Ramlal and Karen Teemul, et al. "Third generation cephalosporin use in a tertiary hospital in Port of Spain, Trinidad: need for an antibiotic policy". *BMC Infect Dis* 4(2004):59.
15. Mehari K. "Evaluation of Ceftriaxone Utilization and Prescriber's Opinion at Armed Forces Referral and Teaching Hospital, Addis Ababa, Ethiopia". 2017.
16. Sewagegn Negese."Evaluation of Ceftriaxone Use for Hospitalized Patients in Ethiopia: The Case of a Referral Hospital". *Int J Pharm Sci &Scient Res* 3(2017):26-31.
17. Koning, S,."Ceftriaxone use in Australian hospitals: results from the 2014 and 2015 Hospital National Antimicrobial Prescribing Survey." *NCAS* .
18. Joynt, GM, J Lipman, C D Gomersall and RJ Young, et al. "The pharmacokinetics of once-daily dosing of ceftriaxone in critically ill patients." *J Antimicrob Chemother* 47(2001):421-429.
19. Patterson Jan E. "Antibiotic utilization: Is there an effect on antimicrobial resistance?." *Chest* 119(2001);4285-4305.

How to cite this article: Azlina Ibrahim, Isa Naina Mohamed, Najma Kori, Chee Lan Lau, Azmi Mohd Tamil, Ramliza Ramli, Petrick Periayasamy. "Evaluation of ceftriaxone use in the medical wards of Universiti Kebangsaan Malaysia Medical Centre (UKMMC) and its outcome". *Clin Infect Dis* 5 (2021): 144