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ORIGINAL ARTICLE

Clinical treatment of pandrug-resistant bacterial infection consulted by clinical pharmacist

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KEYWORDS

Pandrug-resistant bacterial;
Drug therapeutic regimen;
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Abstract *Objective:* Pandrug-resistant (PDR) bacterial infections are associated with considerable prolongation of hospitalization and mortality in clinical practice.

Method: This case-series study was conducted during a 3-year period from 2011 to 2013. A total of 30 PDR patients consulted by clinical pharmacist were recorded to evaluate the anti-infection treatment.

Results: All isolates of PDR bacteria from patients were identified as pan-drug resistant acine-tobacter baumannii (63.3%), pan-drug resistant klebsiella pneumonia (20.0%), and pan-drug-resistant pseudomonas aeruginosa (16.7%). Of the 30 patients, 96.7% therapeutic regimens supposed by clinical pharmacists were applied to treat the infectious patients up to 82.8% clinical cure rates. 30 patients completed the prescribed treatment, of which 19 underwent monotherapy that the clinical cure rate was 78.9%, and 10 underwent combination therapy that the clinical cure rate was 90.0%. In the following therapy, doxycycline, cefoperazone shubatan and amikacin have the certain effect on anti-infection therapy. Combination therapy combined with doxycycline was better treatment option for PDR infectious patients.

Conclusion: In a word, it appears to be effective for the successful therapy of PDR infections upon tetracyclines administration.

1. Introduction

Pandrug-resistant bacterial infection has become a significant public health threat as the pathogenic bacteria can be resistant to multiple antimicrobial agents along with abuse use of broad-spectrum antibiotics in clinical practice. As this problem continues to grow, these organisms have become resistant against all commercially available antimicrobial agents or remain susceptible only to older, potentially more toxic agents such as polymyxins and tigecycline, leaving limited and suboptimal

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options for treatment (Poulikakos et al., 2014; Matthew et al., 2006). PDR gram-negative bacteria, namely acinetobacter baumannii, pseudomonas aeruginosa and klebsiella pneumonia, is widely spread in clinic due to their strong viability, colonization occurrence rate and antibiotic resistance, etc.

Because PDR bacteria easily adopt resistance mechanisms, the controversy surrounds antibiotic options with regard to the effectiveness and susceptibility of resistant strains in clinical practice (Corbella et al., 2000; Oliva et al., 2014). Thereby, it is difficult to define a standardized treatment regimen against PDR bacterial infection in patients.

Our paper is a retrospective study and addresses the matter of optimal treatment for PDR infection, focusing on 30 PDR patients consulted by clinical pharmacist which occurred during a 3-year period from 2011 to 2013. Interestingly, tetracyclines old drug doxycycline, is also applied for combination therapeutic regimen in this study and its effectiveness is 100%.

2. Method

2.1. Patient source

This case-series study was conducted during a 3-year period from 2011 to 2013. A total of 30 PDR patients consulted by clinical pharmacist are recorded in detail, such as laboratory data, diagnosis, drug use before and after consultation and consultation summary.

The pandrug-resistant bacterials in this study are mainly comprised of pandrug-resistant gram-negative bacillus infection, not gram-positive cocci including methicillin-resistant staphylococcus aureus (MRSA) and vancomycin resistant enterococcus (VRE).

2.2. Evaluation of therapeutic efficiency

We evaluate the therapeutic efficiency, according to the standard *Clinical Study Guiding Principles of Antibiotics* published by Ministry of Health in 2004. The criteria are below:

Recovery: recover in symptoms, signs, laboratory examination and etiology; Improvement: get better in the patients, but laboratory data are not fully recovered and the bacteria turns to colonization and asymptomatic; Invalid: no improvement or worse within 72 h after drugs administration (Dong and Dong, 2010).

The following antibiotics were administered to the patients: sulbactam, cefoperazone, imipenem, cystatin, meropenem, amikacin, and doxycycline.

2.3. Data analysis

Data are presented as number (%) for categorical variables and mean value ± standard deviation (SD) for continuous variables. P-values < 0.05 were considered to be significant and all tests were two-tailed.

3. Results

3.1. Patient

The patients are consist of 21 male patients (70%) and 9 female patients (30%). Patient age is range from 43 to 90 years with the average age of 72 years. 17 patients (56%) have pulmonary infection, 6 patients (20%) have urinary system infection, 3 patients (10%) have gallbladder and abdominal infection, and 3 patients (10%) have local wound infection, and 1 patient (3%) has blood infection (Table 1).

3.2. Bacterial distribution

Pan-drug resistant acine-tobacter baumannii, pan-drug resistant klebsiella pneumonia and pandrug-resistant pseudomonas aeruginosa were isolated from patients respectively (Table 2).

Remark: XDRAB means pan-drug resistant acine-tobacter baumannii; XDRKP means pan-drug resistant klebsiella pneumonia; XDRPA means pandrug-resistant pseudomonas aeruginosa.

3.3. Therapeutic regimen and efficacy outcome

In 30 patients of consultation, the clinicians recommend to adopt 29 cases of consultation, only 1 of which is not adopted (Table 3).

In 30 cases of drug use, 1 case is not given antibiotics and the curative effect is improved. In 19 cases of monotherapy, the effective rate is 78.9%, including regimen A: sulbactam and cefoperazone 3 g q8 h ivgtt 9 cases; regimen B: imipenem and cystatin 1 g q8 h ivgtt or meropenem 1 g q8 h ivgtt 7 cases; regimen C: Amikacin 0.4 g qd ivgtt 3 cases. 10 cases combination therapy and the effective rate is 90.0%; regimen D: amikacin 0.4 g qd ivgtt + sulbactam and cefoperazone 3 g q12 h ivgtt 5 cases; regimen E: Amikacin 0.4 g qd ivgtt + imipenem

Table 1 Specimen source of PDR patients.

Specimen	Cases	Ratio (%)
Phlegm	17	56.7
Urine	6	20.0
Drainage liquid	4	3.3
Local secreta	2	6.7
Blood	1	3.33

Table 2 Bacterial species of PDR.

Bacteria	Number of cases	Constituent ratio (%)
XDRAB	19	63.3
XDRKP	6	20.0
XDRPA	5	16.7

Table 3 Clinical reception of therapeutic regimen supported by clinical pharmacist.

Adoption	Cases	Ratio (%)
Full adoption	23	76.7
Adoption + Subsequent adjustment	6	20.0
Not adoption	1	3.3

Table 4 Therapeutic regimens and clinical efficacies of patients.

Therapeutic regimen	Cases	Recovery	Improvement	Non-effective	Effective rate (%)
Monotherapy					
Regimen A	9	1	7	3	
Regimen B	7	3	1	1	
Regimen C	3	1	2	0	
Total	19	5	10	4	78.9
Combination therapy					
Regimen D	5	1	3	1	
Regimen E	2	1	1	0	
Regimen F	3	1	2	0	
Total	10	3	6	1	90.0

and cystatin 0.5 g q8 h ivgtt 2 cases; regimen F: doxycycline 0.2 g q12 h ivgtt + sulbactam and cefoperazone 3 g q12 h ivgtt 3 cases (Table 4).

4. Discussion

Pandrug-resistant bacteria (PDR or XDR) are characterized by the bacterial strain with sensitive to 1–2 potential active drugs or resistant to all current antibacterial agents (Pontikis et al., 2014). In our hospital, pandrug gram-negative bacillus infection bacteria mainly consists of pan-drug acinetobacter baumannii, klebsiella pneumonia and pseudomonas aeruginosa. Pulmonary infection and urinary system infection, as the main infection sites, are up to 80%. 30 cases were observed in this study, 15 cases of which are sensitive to amikacin (or tobramycin) and polymyxin, and 15 cases of which are all drug resistance. Among the 30 patients, 19 patients were applied for mono-therapy with the 78.9% effectiveness, 10 patients accepted combination therapy with the 90.0% effectiveness, and 1 patient is not use any antibiotic drug therapy.

In 19 cases of monotherapy regimens, 16 cases increase the dosage and frequency of β lactam or carbapenem administration, such as cefoperazone sulbactam 3 g q8 h ivgtt, imipenem cystatin 1 g q8 h ivgtt, meropenem 1 g q8 h ivgtt, 12 cases of which are effective and 4 cases of which are non-effective. In addition, 3 cases were used to the only sensitive drug (amikacin 0.4 qd ivgtt), all of which are effective. Considering the polymyxin is unable to obtain in our hospital, amikacin is the only drug with higher sensitive probability among those selective antibiotics. The results confirmed that amikacin has the better antibacterial effect *in vitro* and *in vivo*. As we known, sulbactam and cefoperazone are not listed in the content of sensitivity drug and its sensibility is uncertain. Thus, it was selected empirically from clinical practice (Liang and Liang, 2011) and its usage dose increased. Interestingly, sulbactam and cefoperazone obtain a certain therapeutic effect and their effectiveness is about 88.9%. In a word, sulbactam still has a certain therapeutic effect on pandrug-resistant bacteria, especially for carbapenems resistance acinetobacter (Shiying and Liu, 2006).

In 10 cases of combination regimens, the effective rate reaches 90.0%. Combination regimens respectively are amikacin 0.4 qd ivgtt + sulbactam and cefoperazone 3 g q12 h ivgtt, amikacin 0.4 qd ivgtt + imipenem and cystatin0.5 g q8 h ivgtt, doxycycline 0.2 q12 h ivgtt + sulbactam and cefoperazone 3 g q12 h ivgtt. As reported in mono-therapy, sulbactam-cefoperazone and amikacin have the obvious advantage to recovery patients. In the following combination therapy, amikacin combining with sulbactam–cefoperazone or the other antibiotics is significantly superior to monotherapy regimens. In addition, it has been reported that tetracyclines, as an old drug doxycycline, success in pandrug-resistant acinetobacter treatment (Arroyo et al., 2009). In this study, tetracyclines combining with the other antibiotics reached 100% effectiveness. The tetracyclines administration maybe attribute to the following reason. Tetracycline is little application in the clinical anti-infection treatment, which led to the very low drug resistance to pandrug-resistant acinetobacter infection. Second, the cheap tetracyclines should be considered an alternative to tigecycline with very high price. In terms of drug economics and bacterial resistance, we will pay attention to the therapeutic effects of tetracyclines in the future and accumulate more cases in clinical practice.

A total of 30 PDR patients consulted by clinical pharmacist were conducted during a 3-year period from 2011 to 2013. Of the 30 patients, 96.7% therapeutic regimens supposed by clinical pharmacists were applied to treat the infectious patients up to 82.8% clinical cure rates. Clinical pharmacists have its professional and comprehensive advantage in medicinal property, pharmacological action, pharmacokinetics, interaction, untoward effect, drug efficacy tracking and evaluation (Giamarellou et al., 2013; Miyakis et al., 2011; Tsioutis et al., 2010). Thereby, clinical pharmacists and doctors appear to be effectively collaborative team for the successful treatment of PDR infections.

5. Conclusion

In conclusion, doxycycline, cefoperazone shubatan and amikacin have the certain effect on PDR infectious patients. Combination therapy combined with doxycycline was better treatment option.

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7. Disclosure statement

The authors have nothing to disclose.

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