Use of polymyxin B in patients with renal impairment: A retrospective examination of 5 cases

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Abstract. In order to provide an idea dose of polymyxin B in Chinese patients with renal impairment, the present study collected the clinical data of all patients with renal impairment who received polymyxin B therapy in the intensive care unit (ICU) of The First Affiliated Hospital of Bengbu Medical College (Bengbu, China). The clinical data of six patients treated in the ICU between February 2018 and May 2019 were retrospectively analyzed. All patients had renal impairment and were treated with polymyxin B combination therapy. The patients in the current study received polymyxin B and carbapenem, or polymyxin, carbapenem, cefoperazon and sulbactam, or polymyxin B, carbapenems and aminoglycoside treatment. One patient discontinued treatment. The other five patients received polymyxin B at a dosage of 50 mg every 12 h (100 mg/day) through an intravenous drip. During treatment, four of the five patients had deteriorating renal function to varying degrees, and continuous renal replacement therapy (CRRT) was initiated. Polymyxin B was discontinued in all patients when the infection was controlled. After treatment, four of five patients showed improvement in renal function, and had normal kidney function at the 1-month follow-up evaluation, whereas one patient had chronic renal disease. During hospitalization, one patient experienced neurotoxicity, showing decreased limb muscle strength and cognitive impairment, which might have been caused by polymyxin B, according to the Naranjo adverse drug reactions probability scale (also known as the Naranjo algorithm) score. The present report demonstrated that the administration of 100 mg daily dosage of polymyxin B to the five patients weighing between 50 and 75 kg, could control pulmonary infection during the course of treatment of Chinese patients with renal impairment, however, further research is needed to verify this result. Risk factors for nephrotoxicity and neurotoxicity need to be fully assessed before initiating polymyxin B therapy in patients with renal impairment.

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Introduction

In the 1950s, polymyxins were widely used as antimicrobial agents in the clinical treatment of gram-negative infections. Thereafter, polymyxins were replaced with new antibiotics because of its narrow therapeutic index and the high risk for nephrotoxicity and neurotoxicity (1). Over the past 30 years, few clinical studies have been conducted regarding the antimicrobial spectrum, pharmacokinetics, pharmacodynamics, toxicology and clinical use of polymyxins, especially polymyxin B.

The outbreak of carbapenem-resistant Enterobacteriaceae (CRE) is one of the main reasons for the increased use of polymyxin B (2-4). Most CRE outbreaks in China occur in the intensive care unit (ICU). When the minimum inhibitory concentration (MIC) >4 mg/l, enterobacteriaceae are resistant to carbapenem; the MIC of carbapenem against CRE is usually >16 mg/l, and, therefore, the MIC of carbapenem against CRE is very high (4,5). In addition to CRE, the incidence of pan-drug resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* (MIC values ≥16 mg/l for both) has also gradually increased in the ICU of our hospital (The First Affiliated Hospital of Bengbu Medical College; Bengbu, China) for the past 2 years. Data released by the China Antimicrobial Surveillance Network (CHINET) in 2018 showed that the imipenem resistance rate of *A. baumannii* was as high as 73.2%, whereas resistance rates of *P. aeruginosa* and *Klebsiella pneumoniae* were 30.7 and 37.6%, respectively. Polymyxin B is one of the main drugs used in combination therapy for pan-drug resistant *A. baumannii*, *P. aeruginosa* and *K. pneumoniae*, and has been considered as a treatment of last resort for gram-negative infections (1,6-8).

Polymyxin B was first introduced to the Chinese market in September 2017. Currently, limited clinical data is available with respect to the rational use of polymyxin B in Chinese

patients. As a result, usage and dosage (including calculation and administration of the loading dose) are mainly based on international clinical literature, for example, 1.25-1.5 mg/kg every 12 h (2.5-3 mg/kg daily) by intravenous (i.v.) drip (9-14). Polymyxin B is mainly eliminated by non-renal pathways, and continuous renal replacement therapy (CRRT) has limited effects in the clearance of polymyxin B (14-16). Therefore, the latest International Consensus Guidelines for the Optimal Use of the Polymyxins does not recommend adjusting the loading and maintenance doses for patients receiving CRRT (17). However, given that Chinese people generally weigh significantly less compared with people of other nationalities, additional investigations are required to determine whether the currently recommended dosage of 1.25-1.5 mg/kg every 12 h is suitable for Chinese people, especially for those with renal impairment.

In May 2018, polymyxin B was given to a patient with renal impairment in the ICU of our hospital at a 100 mg daily dose (50 mg/12 h, via i.v. drip; 1.25-1.5 mg/kg) for 24 days. The infection was brought under control and the renal function improved significantly before hospital discharge. Subsequently, all relevant data on the use of polymyxin B in patients with renal impairment treated in our hospital was collected for further analyses. In the present study, clinical data of five patients with renal impairment who received polymyxin B therapy in the ICU of the hospital between February 2018 and May 2019 was analyzed to determine the optimal polymyxin B dosage in patients with renal dysfunction.

Materials and methods

Patients. Clinical data was collected from patients with renal impairment who received polymyxin B therapy in the ICU of our hospital between February 2018 and May 2019. All relevant information, including sex, age, weight were collected from medical records (Table I). Body temperature, procalcitonin (PCT) level, C-reactive protein (CRP) level, white blood cell count, neutrophil count, cystatin C level, creatinine level and urine volume before and after the use of polymyxin B were also recorded. The specific time for the use of CRRT during polymyxin B therapy was also documented. Creatinine clearance was calculated by the following formula: Male, creatinine clearance=(140-age) x body weight (kg)/0.818x creatinine level (μmol/l); female, multiply the result of the male formula by 0.85.

X-ray or CT chest scans. Chest X-rays (AXIOM Luminos *d*RF; Siemens AG) or CT scans (Revolution CT; GE Medical Systems, LLC) were used to determine the status of pulmonary infection.

Muscle strength examination. Muscle strength was manually examined using the 6-grade scoring method, in which the subject takes a standard test position and performs standard test movements. The muscle's ability to complete the movements was observed and, if applicable, the physician would palpate or passively move the patient's hand or foot and judge contraction strength according to patient response. Muscle strength was classified into grades of 0, I, II, III, IV or v, with a total of 6 possible grades. Grade 0 indicated that there was no muscle contraction. Representative symbols (zero, O), rated as: Total paralysis, muscle strength 0% of normal muscle strength. Grade I, there was muscle contraction; however, not enough to allow the joints to move. Representative symbols (trace, T), rated as: Slightly contracted, 10% of normal muscle strength. Grade II, muscle contraction allowed the limb to do full range of joint motion under conditions that remove gravity (the physician would raise the patients' limb and then release to observe whether the patient could move their limb freely). Representative symbol (poor, P), rated as: Poor, 25% of normal muscle strength. Grade III, muscle contraction enabled the limb to resist gravity for full range of joint motion; however, not for added resistance. Representative symbols (fair, F), rated as: Fair, 50% of normal muscle strength. Grade IV, muscle contraction enabled the limb to resist gravity and certain external resistance. Representative symbols (good, G), rated as: Good, 75% of normal muscle strength. Grade V, muscle contraction allowed limb movement to resist gravity and added resistance. The representative symbols (normal, N), rated as: normal, 100% of normal muscle strength.

Results

Basic information of patients. Between February 2018 and May 2019, a total of six patients with renal impairment received polymyxin B combination therapy (age range, 28-74 years; weight, 50-75 kg) in the ICU of our hospital. Patients Nos. 2-6 exhibited infection control following the use of polymyxin B (at 9-24 days post-treatment). Of all six patients, five had acute renal failure caused by infection, and only one patient (patient No. 4) had stage V chronic kidney disease. Table I shows that polymyxin B was used in patients nos. 1-3 primarily due the ascitic fluid, sputum or blood cultures testing positive for carbapenem-resistant *K. pneumoniae*. Polymyxin B was used in patient No. 4 based on clinical experience with patients of immunosuppression (18). Polymyxin B was used in patient No. 5 because the sputum culture tested positive for pan-resistant *P. aeruginosa* (imipenem MIC ≥16 mg/l). In patient No. 6, the sputum culture tested positive for multidrug-resistant *P. aeruginosa* on April 28 and 30 (imipenem MICs were 4 and 8 mg/l, respectively). The patient also had an increased body temperature and elevated levels of PCT and CRP between April 28 and May 2, 2019. Because the patient had typical clinical manifestations of systemic inflammatory response syndrome and a high likelihood of a bloodstream infection, polymyxin B combination therapy was initiated (19). Blood cultures on May 10 and 12 from the same patient confirmed that the patient had *Elizabethkingia meningoseptica* sepsis. The main infection-related diagnoses observed in the six patients included septic shock, pulmonary infections, bloodstream infections, pyemia, and sepsis (Table I).

A 100 mg daily dose of polymyxin B effectively controls infection in five patients with renal impairment. Infections were controlled in patients No. 2-6 with a 100 mg daily dose of polymyxin B. The body weight of patient No. 1 was 70 kg. The patient received polymyxin B according to 1.25-1.5 mg/kg every 12 h (9-14) and, therefore, 87.5-105 mg every 12 h should be given. However, the patient had renal impairment and polymyxin B can induce nephrotoxicity (20,21). Furthermore, the

Table I. Basic information of the six patients.

Patient number	Sex	Age (years)	Weight (kg)	Main clinical diagnosis	Primary positive results from culture tests
1	Male	74	70	1. Septic shock 2. Pulmonary infection 3. Bloodstream infection 4. Acute renal failure	On February 20 and 25, blood culture analyses and on February 22 and 24, sputum culture analyses detected *Klebsiella pneumoniae* (pan-drug resistant bacteria; imipenem MIC ≥16 mg/l).
2	Male	41	70	1. Multiple injuries 2. Multiple organ failure (acute respiratory distress syndrome; acute renal failure; abnormal coagulation function) 3. Pulmonary infection 4. Pyemia	On May 10, 16 and 17, sputum culture detected *Klebsiella pneumoniae* (pan-drug resistant bacteria; imipenem MIC ≥16 mg/l).
3	Male	55	75	1. Severe acute pancreatitis 2. Multiple organ failure (respiratory failure, acute hepatic injury, acute renal failure) 3.Spectic shock	On August 17, ascitic fluid culture detected *Klebsiella pneumoniae* (pan-drug resistant bacteria, imipenem MIC ≥16 mg/l).
4	Female	56	57.8	1. Chronic renal disease stage V (on maintenance hemodialysis) 2. Pulmonary infection 3. Respiratory failure 4.Chemotherapy-induced myelosuppression 5. Multiple myeloma	Multiple blood and sputum cultures showed no bacterial growth.
5	Male	67	70	1. Gastrointestinal bleeding 2. Pulmonary infection 3. Heart failure 4. Acute renal failure	On March 31, and April 7 and 9, sputum cultures detected *Pseudomonas aeruginosa* (pan-drug resistant bacteria; imipenem MIC ≥16 mg/l).
6	Female	28	50	1. Fulminant myocarditis 2. Cardiogenic shock 3. Acute heart failure 4. Pulmonary infection 5. Sepsis 6. Multiple organ failure (acute respiratory failure; hepatic injury; acute renal failure) 7. Intensive care unit-acquired muscle weakness	On April 28 and 30, sputum culture detected multidrug-resistant *Pseudomonas aeruginosa* (imipenem MIC=4 mg/l on April 28; imipenem MIC=8 mg/l on April 30). On 10 and 12 May, blood culture detected *Elizabethkingia meningoseptica* (multi-drug resistant bacteria; imipenem MIC ≥16 mg/l).

MIC, minimum inhibitory concentration.

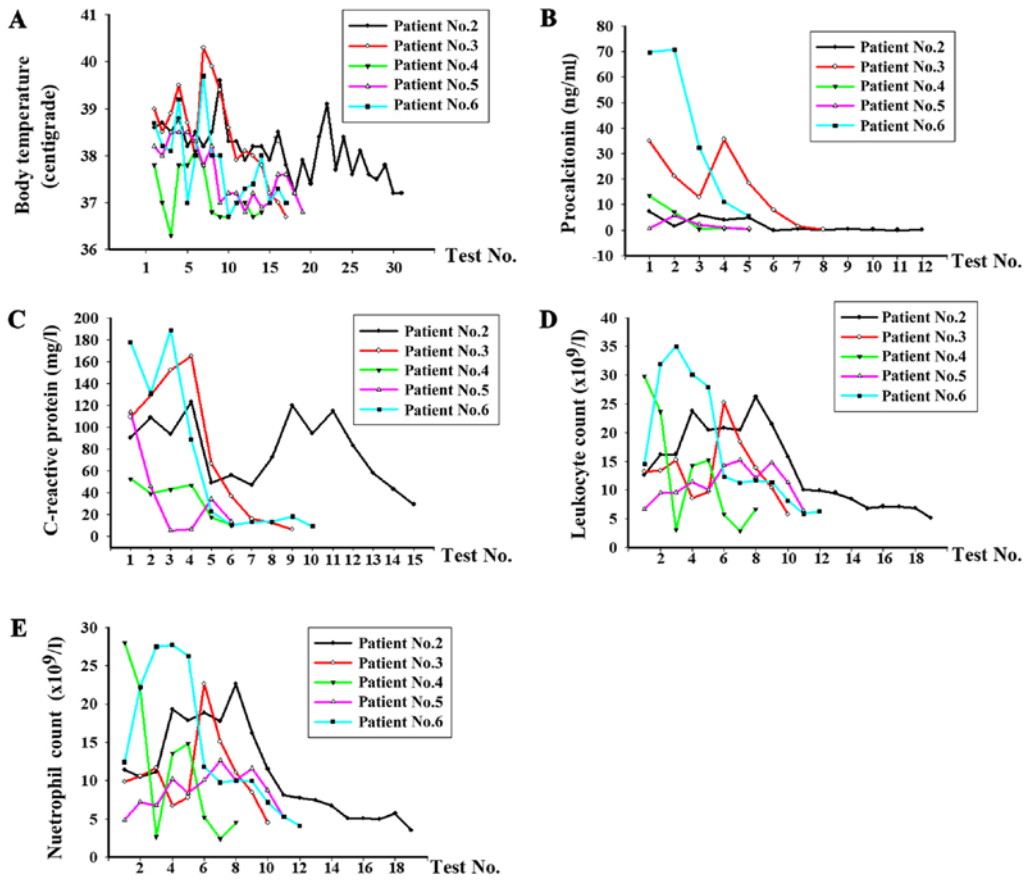

Figure 1. Changes in body physical and chemical parameters before, during and after polymyxin B therapy in patients No. 2-6. (A) Changes in body temperature. (B) Changes in procalcitonin levels. (C) Changes in C-reactive protein levels. (D) Changes in leukocyte counts. (E) Changes in neutrophil counts. The x-axis indicates the test times for the above parameters.

use of 1.25-1.5 mg/kg every 12 h in patients with renal impairment are not based on Chinese data (9-14). Therefore, the current study administered 50 mg every 12 h for patient No. 1. However, family members of the patient decided to discontinue treatment after 5 days of polymyxin B therapy. The body weight of patient No. 2 was also 70 kg and 50 mg every 12 h of polymyxin B for 24 days was administered and the infection was controlled.

The patients had a notable decrease in body temperature, white blood cell count, neutrophil count, PCT level and CRP level during polymyxin B therapy (Fig. 1). Prior to polymyxin B treatment, the average body temperature was 38.5˚C and decreased to 36.9˚C (normal body temperature range, 36.1-37˚C) following polymyxin B therapy. The average level of procalcitonin was 14.9 ng/ml prior to treatment and decreased to 1.4 ng/ml (normal procalcitonin, <0.5 ng/ml). The average level of c-reactive protein of patients No. 2-6 was 112.5 mg/l prior to treatment and decreased to 15.3 mg/l (normal c-reactive protein range, 0-10 mg/l) when the infections were controlled. The average leukocyte count (normal leukocyte count range, 4-10x10^9/l) were prior to treatment 21.7x10^9/l and decreased to 5.3x10^9/l. Additionally, the average neutrophil count (normal neutrophil count range, 2-7x10^9/l) decreased from 19.1x10^9/l to 3.9x10^9/l. X-ray or CT chest scans of the five patients before and after treatment also showed that pulmonary infection was controlled (Fig. 2).

With the exception of patient No. 4, who had stage V chronic renal disease, the renal function of the remaining patients' improved when the infections were controlled and received supportive treatment using CRRT, as demonstrated by elevated creatinine clearance, urine volume and decreased levels of cystatin C and urea (Fig. 3B and C). Prior to polymyxin B treatment, the average creatinine clearance was 21.6 ml/min and increased to 58.7 ml/min (normal creatinine clearance range, 80-120 ml/min) following polymyxin B therapy. The average level of cystatin C was 6.4 mg/l before treatment and decreased to 2.4 mg/l (normal cystatin C range, 0.6-1 mg/l). The average level of urea decreased from 30.1 to 12.1 mmol/l. Additionally, the urine volume of patient No. 2, 3, 5 and 6 improved following the infection control and were 2,675, 2,520, 3,260, 2,100 ml (normal urine volume range, 1,500-1,800 ml/24 h), respectively (Fig. 3D).

Changes in creatinine clearance and polymyxin B treatment in the five patients (patients No. 2-6) while on polymyxin B therapy were measured (Fig. 4). The creatinine clearance rate decreased in patient No. 2 on May 13 and decreased again from May 17-24, however, the creatinine clearance rate increased markedly after May 25. This increase was observed following supportive treatment using CRRT was provided between May 11 and 25. Creatinine clearance changes were similar for the other three patients No. 3, 5 and 6. The creatinine clearance rates increased to varying degrees after infection was controlled and polymyxin B was discontinued. For patient No. 4 with stage V chronic renal disease, and the creatinine clearance first showed an extremely sharp drop, then

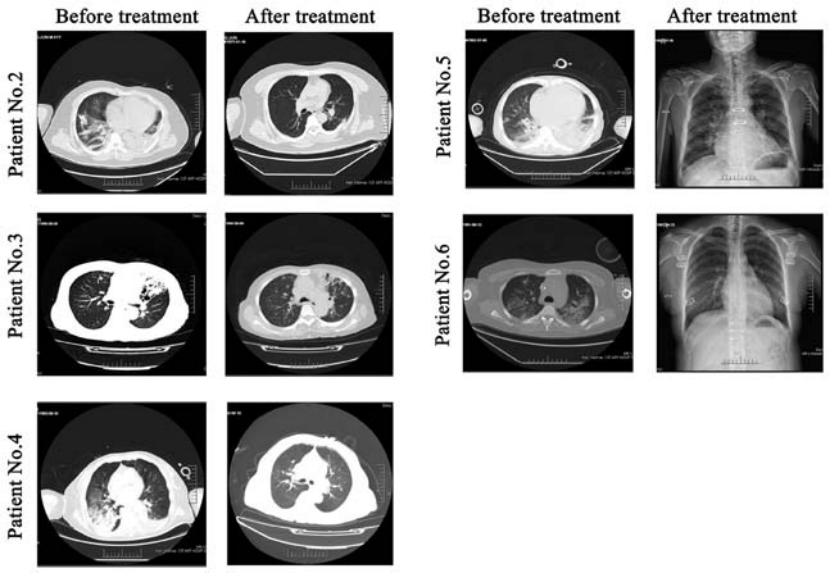

Figure 2. X-ray or CT scans chest of the five patients before and after treatment showed that pulmonary infection was controlled.

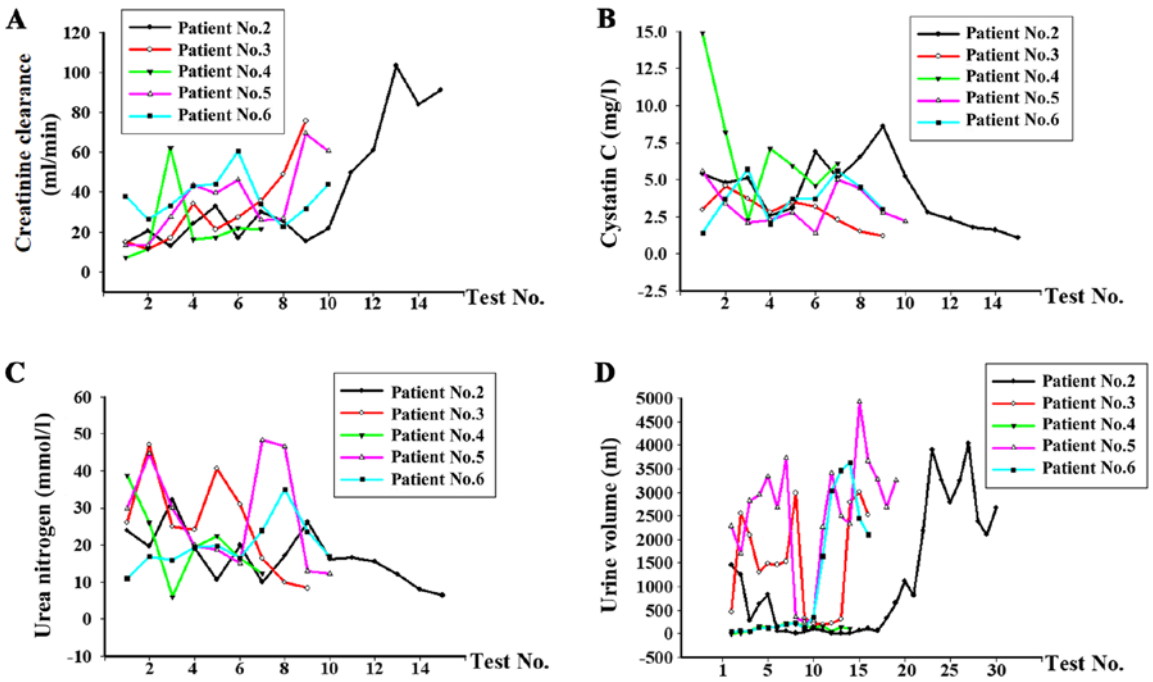

Figure 3. Changes in creatinine clearance, cystatin C level, urea level and urine volume before, during, and after polymyxin B therapy in patients No. 2-6. (A) Changes in creatinine clearance. (B) Changes in cystatin C levels. (C) Changes in urea levels. (D) Changes in urine volume. The x-axis indicates the test times for the above parameters.

increased following CRRT supportive treatment. Additionally, the results demonstrated that, during polymyxin B therapy, the five patients had similar trends in creatinine clearance as in clearance first decreased, then increased by varying degrees (Fig. 4).

Of the five patients in whom the infections were controlled, four had normal renal function at the 1-month follow-up evaluation and patient No. 4 remained with stage V chronic kidney disease. These results suggested that a 100 mg daily dose of polymyxin B was effective in controlling infections in patients with renal impairment (weight range, 50-75 kg), and CRRT could be used as a supportive treatment for deteriorating renal function during polymyxin B therapy.

Neurotoxicity in patient No. 6 was likely caused by polymyxin B. Patient No. 6, a 28-year-old female with fulminant myocarditis, was administered polymyxin B combination therapy from May 3-12, 2019. On May 5, the lower extremity muscle strength decreased to grade III. On May 10, the lower extremity muscle strength decreased to grade II. On 13 May, the lower extremity muscle strength decreased to grade I and the upper extremity muscle strength decreased to grade IV. In addition, on May

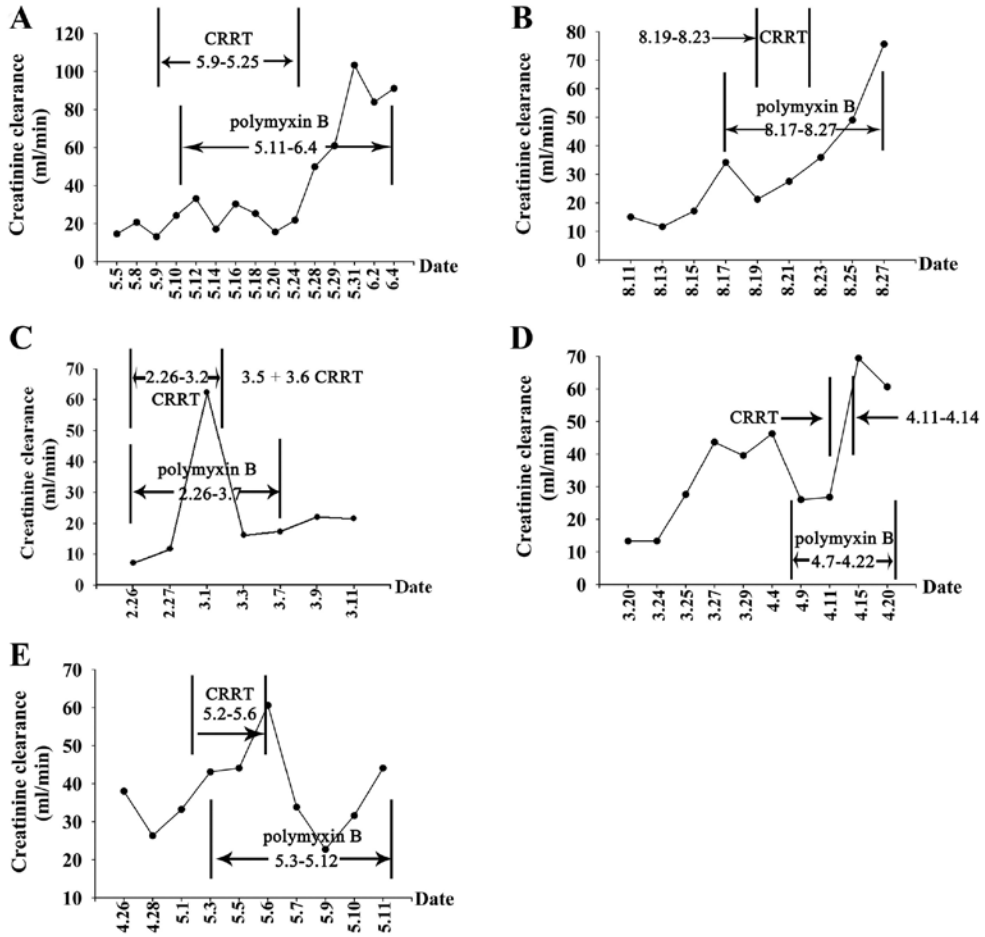

Figure 4. Changes in creatinine clearance during polymyxin B therapy in patients No. 2-6. (A) Changes in creatinine clearance in patient No. 2 between May 5 and June 4. Polymyxin B was administered between May 11 and June 4, and CRRT was administered May 9-25. (B) Changes in creatinine clearance in patient No. 3 on August 11-27. Polymyxin B was administered August 11-27 and CRRT was given from August 19-23 during polymyxin B therapy. (C) Changes in creatinine clearance in patient No. 4 between February 26 and March 11. Polymyxin B was administered between February 26 and March 7, and CRRT was administered between February 26 to March 2, and again on March 5-6 during polymyxin B therapy. (D) Changes in creatinine clearance in patient No. 5 between March 20 and April 20. Polymyxin B was administered April 7-22 and CRRT was administered April 11-14 during polymyxin B therapy. (E) Changes in creatinine clearance in patient No. 6 from April 26 to May 11. Polymyxin B was administered from May 3-12, and CRRT was given from May 2-6 during polymyxin B therapy. CRRT, continuous renal replacement therapy.

13, the patient experienced transient cognitive impairment and could not recall her name or her marital status. Her cognition returned to baseline spontaneously later that day. On May 13, the patient underwent an electromyogram (EMG) examination, which includes results of motor nerve conduction, sensory nerve conduction and F-waves. The motor nerve conduction study showed that the compound muscle action potential amplitude of the left and right common peroneal nerves decreased (Table SI). The results of the sensory nerve conduction study were all normal (Table SI). The F-wave study showed that the occurrence rate and latency of F-waves in the left median nerve and left and right posterior tibial nerves were normal (Table SII). The EMG results (Table SIII) showed the presence of spontaneous potentials in the left and right tibialis anterior muscles, right extensor digitorum brevis muscle, left and right biceps femoris muscles, and right L4 paraspinal muscle and their inability to contract. The left and right gastrocnemius muscles, right peroneus longus muscle and right vastus medialis muscle did not show spontaneous potentials and were unable to contract. The EMG findings concluded that the patient had neurogenic damage involving both lower extremities.

It is widely accepted that decreased muscle strength and cognitive impairment are manifestations of neurotoxicity induced by polymyxin B (20,21). Patient No. 6 had a total Naranjo adverse drug reactions probability scale (Naranjo algorithm) score of 5, which indicated that the adverse drug reactions in question were probably caused by polymyxin B (22,23). Table II shows the specific questions and the corresponding point values of the Naranjo algorithm. Clinical data suggest that some risk factors, such as drug exposure (the use of polymyxin B in this case), hypoxia, female sex and renal injury, as well as the concomitant use of muscle relaxants, sedatives, anesthetics and corticosteroids, can increase risk for neurotoxicity after use of polymyxin B (20,21). This female patient with renal impairment was treated with polymyxin B from May 3-12, during which time injections of sufentanil citrate, an anesthetic, and methylprednisolone sodium succinate, a class of corticosteroid, were also used (Table III). Therefore, it is important that clinicians closely monitor and assess the risk factors for adverse reactions of polymyxin B, especially in patients with renal injuries.

Table II. Naranjo adverse drug reactions probability scale for patient number 6.

Questions	Question point values			Reasons for the specific point(s) given
	Yes	No	Don't know	
1. Are there previous conclusive reports on this reaction?	+1	0	0	There are already reports of neurotoxicity caused by polymyxin B (+1).
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	The patient showed symptoms of decreased limb muscle strength and cognitive impairment after the use of polymyxin B (+2).
3. Did the adverse event improve when the drug was discontinued, or a specific antagonist was administered?	+1	0	0	The patient restarted to walk on June 10 and climbed stairs on June 19 during follow-ups after polymyxin B was discontinued. On May 13, the result of EMG showed that the patient had neurogenic damage involving both lower extremities. On June 19, no EMG abnormalities were noted during the follow-up (+1).
4. Did the adverse event reappear when the drug was re-administered?	+2	-1	0	Polymyxin B was not re-administered to the patient (+0).
5. Are there alternative causes that could on their own have caused the reaction?	-1	+2	0	No other causes alone can induce the adverse drug reaction for this patient (+0).
6. Did the reaction reappear when a placebo was given?	-1	+1	0	The patient did not take any placebos (+0).
7. Was the drug detected in the blood or other fluids in concentrations known to be toxic?	+1	0	0	The concentration of polymyxin B was not measured (+0).
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	The patient received consistent dose of polymyxin B during the course of the treatment (+0).
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	The patient had not previous exposure to the same or similar drugs (+0).
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	Physical examination during hospitalization showed progressive decrease in muscle strength of both lower extremities. On May 3, the patient was given the first dose of polymyxin B. On May 5, muscle strength of both lower extremities decreased to grade III; on May 10, muscle strength of both lower extremities decreased to grade II; on May 13, muscle strength of both lower extremities decreased to grade I, and that of both upper extremities dropped to grade IV. Also, on May 13, the result of EMG showed that the patient had neurogenic damage involving both lower extremities (+1).
Total score	5	0	0	5

Total Naranjo algorithm score ≧9, indicates adverse reaction is definitely caused by the drug. A score between 5 and 8, indicates adverse reaction is probably caused by the drug. A score between 1 and 4, indicates adverse reaction is possibly caused by the drug. EMG, electromyogram.

Discussion

Of the six patients with renal impairment reported herein, one patient discontinued treatment and the infections of the other five patients were controlled with polymyxin B therapy (50 mg every 12 h, i.v. drip). Supportive CRRT during polymyxin B therapy was also required. The clinical data from the present report provided a reference for the use of polymyxin B in Chinese patients with renal impairment (weight range, 50-75 kg), but further confirmation is needed.

The International Consensus Guidelines for the Optimal Use of the Polymyxins recommends a polymyxin B dose

Table III. Risk factors for neurotoxicity in patient No, 6.

Risk factors	Details
Drug exposure	The patient was given polymyxin B 3-12 May 2019.
Sex	The patient is female.
Concomitant use of anesthetics	Sufentanil citrate injection was administered (300 mg i.v. pump per day) 1-5 May 2019.
Concomitant use of glucocorticoids	Methylprednisolone sodium succinate for injection was administered (80 mg i.v. drip per day) 2-5 May 2019.
Renal injury	The patient had renal injury during polymyxin B therapy.

I.v., intravenous.

of 1.25-1.5 mg/kg every 12 h for patients with severe infections (17), which is supported by many studies (9-14). Low dose polymyxin B is an independent risk factor for treatment failure and death (9-11). Rigatto *et al* (11), showed that polymyxin B is primarily eliminated via non-renal pathways and renal replacement therapy is unlikely to remove a large percentage of polymyxin B from the body. Therefore, in accordance with the International Consensus Guidelines for the Optimal Use of the Polymyxins recommendations, daily doses of polymyxin B should not be adjusted in patients with renal impairment (14-17). Furthermore, a total daily dose >200 mg was associated with a lower risk of mortality, suggesting that an adequate daily dose of polymyxin B is needed to treat patients with severe infections (14-17). However, additional research is needed to define the safety and efficacy of high dose polymyxin B regimens and ensure that an appropriate balance between safety and efficacy is achieved, as nephrotoxicity and neurotoxicity are frequent occurrences with polymyxin B therapy, especially in patients with renal impairment.

By analyzing the clinical data of the five patients in this study, a common characteristic was identified among patients. Four of the patients (except for the patient with chronic kidney disease) had different degrees of deteriorating renal function after the use of polymyxin B. There was reason to believe that this worsening renal function was either infection-induced or caused by polymyxin B. Tests have been performed to further measure multiple organ failure scores in the five studied patients to judge if the increased renal dysfunction was caused by the progress of the multiple organ failure, or caused by the nephrotoxicity induced by polymyxin B. However, a common association has not been found, and therefore, a subsequent study will aim to collect more detailed information from patients to understand if there is an association between organ failure and worsening renal function, that is independent from polymyxin B treatment.

It has been shown that for patients with renal impairment, 36% will experience deteriorating renal function when on polymyxin B therapy (21). The main independent risk factor for renal function damage caused by polymyxin B is the dosage, with a higher dose corresponding to a higher risk of renal function damage (20,21,24). However, infection was controlled for the four patients after CRRT was given, renal function also improved after discontinuing polymyxin B. The patient with chronic kidney disease (patient No. 4), who also received CRRT during polymyxin B therapy, presented reduced levels of cystatin C and urea. The patient's creatinine clearance first exhibited an extremely sharp drop and then increased following CRRT supportive treatment. These clinical data suggest that CRRT is warranted to ensure the safety of polymyxin B therapy for patients with renal impairment.

Patient No. 6 developed limb muscle weakness and temporary cognitive impairment during polymyxin B therapy. She also had a total Naranjo algorithm sore of 5, indicating these adverse reactions were probably caused by polymyxin B. The patient could ambulate on June 10 (27 days after discontinuing polymyxin B) and climb stairs on 19 June. She also exhibited normal limb muscle strength during follow-up evaluations. These results are consistent with clinical literature (18,19). The adverse reactions induced by polymyxin B were reversible, as evidenced by the recovery of cognitive function and limb muscle strength. Therefore, as with vancomycin (25), amikacin (26) and linezolid (27), it is necessary to monitor the concentration of polymyxin B in the blood to explore a safe and effective plasma concentration range, which can lower the incidence of adverse reactions while controlling infection.

In the present report, a 100 mg daily dose of polymyxin B controlled the infections among the five patients examined. This daily dose is relatively low compared with the recommended daily dose by other clinical studies. The reasons for the difference could be that Chinese are generally much thinner and shorter than their western counterparts, with the five reported patients weighting between 50 and 75 kg. However, further research is needed to determine whether the 100 mg daily dose is suitable for patients who weigh more. In addition, despite the relatively low daily dose of polymyxin B, the clinical data of the five patients showed that renal toxicity and neurotoxicity caused by polymyxin B should be a focus on future clinical studies. The current report was limited by the number of cases presented. However, in future clinical work, the safe use of polymyxin B in Chinese patients with renal impairment will continue to be explored in an effort to offer guidance for the optimal clinical use of polymyxin B.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

MY, QW and XH designed the current retrospective study. HW, SYZ and JX were responsible for acquisition of data. XD, SZ and CL analyzed data and constructed the graphs. MY and QW wrote the manuscript, QW and XH revised the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The current study was approved by the Ethics Committee of The First Affiliated Hospital of Bengbu Medical College. All patients provided written informed consent.

Patient consent for publication

All patients provided written informed consent and approved the publication of data.

Competing interests

The authors declare that they have no competing interests.

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