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Factors Affecting the Colistin Nephrotoxicity: Advanced Age and/or Other Factors?

Kolistin Nefrotoksisitesini Etkileyen Faktörler: İleri Yaş mı, Diğer Faktörler mi?

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Abstract

Introduction: The population is aging, and older adults comprise most patients in the intensive care units. Colistin (COL) has been re-introduced to treat increasingly common resistant Gram-negative bacterial infections. Our study aims to investigate the factors affecting COL nephrotoxicity in a general population and geriatric age group.
Materials and Methods: This retrospective study included 170 patients, a total of 116 (68.2%) of whom were in the geriatric group (age ≥65). Acute renal failure was evaluated using the RIFLE score. Factors associated with COL nephrotoxicity were described firstly in a general population and then in the geriatric group patients.
Results: Advanced age [Odds ratio (OR): 1.043; 95% confidence interval (CI): 1.018-1.068; p=0.001] and initial serum creatinine level (OR: 23.122; 95% CI: 3.123-171.217; p=0.002) were found to be the independent risk factors associated with nephrotoxicity. In the evaluation of the geriatric population based on nephrotoxicity, the initial serum urea and creatinine levels, and overall mortality rates were found to be statistically significantly higher in the group with nephrotoxicity (p<0.05). Initial serum creatinine level (OR: 22.48; 95% CI: 2.835-178.426; p=0.003) and concomitant nephrotoxic agent use (OR: 2.516; 95% CI: 1.275-4.963; p=0.008) were independent risk factors associated with nephrotoxicity in geriatric patients.
Conclusion: Advanced age was found to be a risk factor for COL nephrotoxicity. Closed observation should be done especially in the geriatric patients who have initial serum creatinine levels close to the upper limit, concomitant use of the nephrotoxic drugs should be avoided, and if possible, evaluation should be made in terms of non-COL treatment options in these patients.
Keywords: Colistin, nephrotoxicity, geriatric patient, intensive care unit

Öz

Giriş: Nüfus yaşlanmakta ve yoğun bakım ünitelerindeki hastaların çoğunluğunu yaşlı erişkinler oluşturmaktadır. Kolistin, giderek yaygınlaşan dirençli Gram-negatif bakteriyel enfeksiyonları tedavi etmek için yeniden kullanılmaya başlanmıştır. Çalışmamızda genel popülasyonda ve geriatrik yaş grubunda kolistin nefrotoksisitesini etkileyen faktörlerin araştırılması amaçlanmaktadır.
Gereç ve Yöntem: Bu retrospektif çalışmaya 116'sı (%68,2) geriatrik grupta (yaş ≥65) olmak üzere toplam 170 hasta dahil edildi. Akut böbrek yetmezliği RIFLE skoru kullanılarak değerlendirildi. Kolistin nefrotoksisitesi ile ilişkili faktörler önce genel popülasyonda daha sonra geriatrik hastalarda tanımlandı.
Bulgular: İleri yaş [Odds oranı (OR): 1,043; %95 güven aralığı (GA): 1,018-1,068; p=0,001] ve tedavi başındaki serum kreatinin değeri (OR: 23,122; 95% GA: 3,123-171,217; p=0,002) nefrotoksisite ile ilişkili risk faktörleri olarak tanımlandı. Geriatrik popülasyonun nefrotoksisite bazlı değerlendirilmesinde, nefrotoksisitesi olan grupta tedavi başındaki serum üre ve kreatinin düzeyleri ile genel mortalite oranları istatistiksel olarak anlamlı yüksek bulundu (p<0,05). Tedavi başındaki serum kreatinin düzeyi (OR: 22,48; 95% GA: 2,835-178,426; p=0,003) ve eş zamanlı nefrotoksik ilaç kullanımı (OR: 2,516; 95% GA: 1,275-4,963; p=0,008) geriatrik hastalarda nefrotoksisite ile ilişkili bağımsız risk faktörleri olarak saptandı.
Sonuç: İleri yaş, kolistin nefrotoksisitesi için bir risk faktörü olarak bulundu. Özellikle başlangıç serum kreatinin düzeyleri üst sınıra yakın olan geriatrik hastalarda dikkatli olunmalı, nefrotoksik ilaçların eş zamanlı kullanımından kaçınılmalıdır ve mümkünse bu hastalarda kolistin dışı alternatif tedavi seçenekleri açısından değerlendirme yapılmalıdır.
Anahtar Kelimeler: Kolistin, nefrotoksisite, geriatrik hasta, yoğun bakım ünitesi

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Introduction

The number of people aged ≥65 years is increasing globally. With aging, the incidence of chronic disease and malignancy rises, and a decline in the physiologic and immune functions increases susceptibility to infections[1]. Healthcare-associated bacterial infections in old age are particularly alarming because patients >65 of age are more frequently hospitalized and subjected to invasive procedures.

There has been a significant increase in the infections caused by resistant Gram-negative microorganisms. The lack of new drugs effective in the treatment of resistant infections has led to the reintroduction of colistin (COL), which was largely abandoned in a clinical practice due to its nephrotoxic and neurotoxic adverse effects[2-4]. Being treated in the intensive care units (ICUs), and older age are the factors that increase the frequency of infections caused by the resistant microorganisms and complicate the management of the antimicrobial agents used. Some studies have shown that the COL nephrotoxicity increases with age, while no relationship between age and COL-related renal toxicity was detected in others[5-9]. The present study aimed to identify the risk factors associated with COL nephrotoxicity in the general population and geriatric patients hospitalized in the ICUs of our hospital.

Materials and Methods

Study Design and Patient Population

The study was planned as a retrospective cohort study and included 170 adult patients (age ≥18 years) who were followed in the ICU and received a COL intravenously for documented resistant Gram-negative bacterial infections in the Niğde Ömer Halisdemir University Training and Research Hospital between January 1st, 2012 and December 31st, 2019. We investigated the risk factors associated with COL nephrotoxicity in the general population and geriatric patients.

Exclusion criteria were as follows: Patients who received COL for <72 hours; age <18 years; pregnancy; and acute and chronic renal failure at the beginning of a COL treatment. For patients who had received multiple courses of COL therapy, only the first COL treatment was included in the study.

The pharmaceutical preparation of a COL used by the patients was Colimycin® (Kocak Farma, İstanbul, Turkey). One vial contains colistimethate sodium equivalent to the 150 mg of COL base activity. A loading dose of 5 mg/kg was administered to all the patients regardless of the creatinine clearance. For the patients with a creatinine clearance ≥70 ml/min, the total daily dose was calculated as 5 mg/kg/day and administered in two equal doses. The glomerular filtration rate (eGFR) of the patients was monitored under a treatment, and the dose was adjusted according to the eGFR levels.

Data Collection

Demographic characteristics, laboratory data, and information regarding the comorbidities, concomitant use of nephrotoxic and vasopressor agents were collected retrospectively from the infection control committee documents and patients' medical records available in the hospital.

Definitions

Nephrotoxicity was evaluated according to the RIFLE (Risk, Injury, Failure, Loss, End-stage kidney disease) criteria based on the serum creatinine concentrations. According to this system, risk (R) is defined as a 1.5-fold increase in the serum creatinine concentration, injury (I) as a 2-fold increase in the serum creatinine concentration, and failure (F) as a 3-fold increase in serum creatinine or concentration ≥4 mg/dl; loss (L) is defined as persistent acute renal failure >4 weeks, and end-stage renal disease (E) is defined as persistent failure >3 months[10]. Infection was diagnosed according to the criteria defined by the Centers for Disease Control and Prevention[11]. Urea and creatinine concentrations on the first day of the COL therapy were accepted as initial values. In patients with nephrotoxicity, the dose of a COL was adjusted according to the creatinine clearance. Urea and creatinine concentrations on the day of discontinuation of a COL treatment were evaluated as the end-of-treatment values.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) statistics version 18.0 (SPSS Inc. 1989, 2010) software was used to analyze the data. The Shapiro-Wilk test was used to assess the normality of data distribution. The homogeneity of variance was evaluated using a Levene test. Groups were compared using the chi-square or Fisher's exact test for categorical variables, and the independent-samples t-test and Mann-Whitney U test were used for the continuous variables. Quantitative variables were shown as mean±standard deviation or median (minimum-maximum), and categorical variables as number (n) and percentage (%). Potential factors for the COL nephrotoxicity identified by the univariate analyses were analyzed using a multiple logistic regression model. The variables were examined using the Odds ratio (OR) with 95% confidence intervals (CI), and p values <0.05 were accepted as significant.

Results

A total of 170 patients were included in the study (98 men, 57.6%). The median age was 73 (range, 18-95) years. All patients had infections caused by the extremely drug-resistant Gram-negative bacterial infections. The causative bacteria were the

Acinetobacter baumannii (78.2%), *Klebsiella pneumoniae* (15.9%), and *Pseudomonas aeruginosa* (5.9%). Totally 108 (63.5%) patients had a lower respiratory tract infection, 48 (28.2%) had bloodstream infection, 8 (4.7%) had surgical site infection, and 6 (3.5%) had a urinary tract infection.

Nephrotoxicity was detected in the 106 (62.4%) patients. According to the RIFLE classification, 18 (10.6%) patients were evaluated in the "risk" group, 36 (21.2%) patients in the "injury" group, and 52 (30.6%) patients in the "failure" group. Sixty-four patients had no risk factors for the development of nephrotoxicity. Five (4.7%) of the patients who developed nephrotoxicity required hemodialysis. Nephrotoxicity classification of an elderly and young patients according to the RIFLE score is shown in Figure 1.

The median age of the patients who developed nephrotoxicity was 75 years (range, 19-95) and 50% were male. The duration of the hospitalization before a COL therapy was similar in patients with and without nephrotoxicity (p=0.109). The prevalence of chronic obstructive pulmonary disease (COPD) was significantly higher in the nephrotoxicity group (p=0.02), but there was no significant difference found between the two groups in terms of other comorbid diseases. Initial serum urea and creatinine levels were significantly higher in the nephrotoxicity group (p<0.001). APACHE II score, vasopressor agent use, concomitant nephrotoxic agent use, 28-day mortality, and the overall mortality rates were also higher in nephrotoxicity group (p<0.05). The demographic, clinical, and laboratory characteristics of the patients based on nephrotoxicity are given in Table 1.

In a multivariable logistic regression analysis, advanced age (OR: 1.043; 95% CI: 1.018-1.068; p=0.001) and initial serum creatinine levels (OR: 23.122; 95% CI: 3.123-171.217; p=0.002) were found to be independent risk factors associated with nephrotoxicity (Table 2).

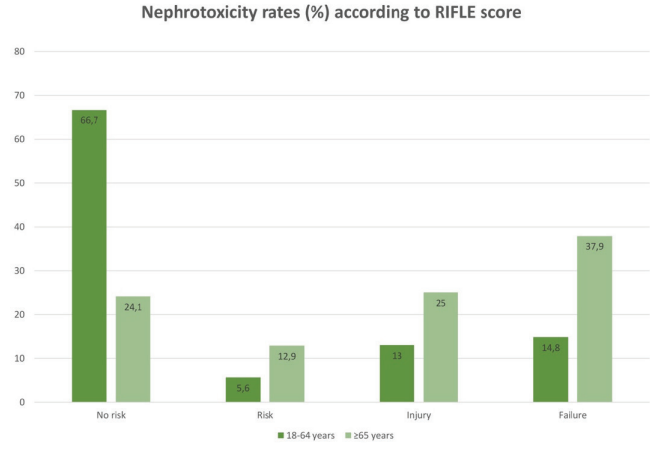

Figure 1. Age-based nephrotoxicity rates according to RIFLE score

RIFLE: Risk, Injury, Failure, Loss, End-stage kidney disease

Nephrotoxicity was observed in 88 of the patients aged ≥65 years. When the patients in the geriatric age group were compared based on nephrotoxicity, the initial serum urea and creatinine values, concomitant nephrotoxic agent use, and the overall mortality rates were found to be statistically higher in the patients with nephrotoxicity (p<0.05) (Table 3). In the same patients' group, initial serum creatinine level (OR: 22.489; 95% CI: 2.835-178.426; p=0.003) and concomitant nephrotoxic agent use (OR: 2.516; 95% CI: 1.275-4.963; p=0.008) were identified as independent risk factors associated with nephrotoxicity (Table 4).

Comparison between the younger and older patients who developed nephrotoxicity showed that the older group had a significantly higher APACHE II score, vasopressor agent use, and 14-day, 28-day, and overall mortality rates (p<0.05) (Table 5). There was no significance between the two groups in terms of initial and end-treatment serum urea and creatinine levels, concomitant nephrotoxic agent use, and hemodialysis need found.

Discussion

Colistin is a cationic polypeptide-based antimicrobial agent that was first used in the 1950s but was restricted in the 1970s due to its adverse effects[12]. The recent dramatic increase in resistant Gram-negative bacterial infections has led to the resurgence of a COL, especially in the ICUs. Colistin-associated nephrotoxicity remains a major problem in clinical use, and the incidence is reported to vary widely, between 11 and 76%[3,7,8,13,14]. In our study, the acute renal failure rate was determined as 62.4%. Although most of our patients were evaluated as "failure" or "injury," only five of the patients required hemodialysis. Several factors have been associated with COL nephrotoxicity in the literature, such as higher APACHE II score, hypoalbuminemia, basal serum creatinine concentration, concomitant nephrotoxic drug use, and sex[3,6-8]. In the present study, we determined that age, APACHE II score, initial serum creatinine concentration, and the rate of concomitant nephrotoxic agent use, were higher among patients who developed nephrotoxicity and that the female sex carried a greater risk than the male sex. Like our results, there are studies in the literature that identify advanced age as a risk factor for COL nephrotoxicity[15,16].

Most of the patients treated with a COL in this study were older patients. Although the rate of COL nephrotoxicity was found to be higher in the patients with underlying chronic diseases[5,17], when our patient population was evaluated from this point of view, COPD was found significantly higher in the geriatric group. Aydoğan et al.[5] reported higher rates of cardiac disease and COPD in the geriatric group, but it was found that the advanced age is not a risk factor for nephrotoxicity. In our study, no significant difference was found between the geriatric

and young patients who developed nephrotoxicity in terms of the concomitant nephrotoxic agent use, initial serum urea, and creatinine values. These results have enabled us to evaluate the risk factors associated with nephrotoxicity in the geriatric patients more objectively. When the literature is reviewed, there is no study investigating the risk factors associated with COL nephrotoxicity in the geriatric group, which constitutes most of the patient population followed up in the ICU.

We also observed that the concomitant use of nephrotoxic agents was more common in the nephrotoxic group in this study. The high incidence of cardiac disease in geriatric patients increases the use of agents such as ACE inhibitors and furosemide in this group. In addition to impaired renal function, hyperkalemia is an important adverse effect of ACE inhibitors[18]. Loop diuretics such as furosemide are also frequently used in ICU patients. These agents cause volume depletion with an excess diuresis, causing hypotension and acute renal failure. Close monitoring of the electrolyte levels and symptoms of hypotension and dehydration is necessary for ICU patients, especially those using the concomitant nephrotoxic agents.

Several studies have evaluated the time from the COL initiation to the appearance of a COL-associated nephrotoxicity. One of

Table 1. Demographic, clinical, and laboratory features of all the patients according to nephrotoxicity

Variables	Nephrotoxicity (+) n=106 (62.4%)	Nephrotoxicity (–) n=64 (37.6%)	p value
Age, median (min-max)	75 (19-95)	62 (18-92)	**<0.001**
Sex, n (%)			
Male	53 (50)	45 (70.3)	**0.009**
Female	53 (50)	19 (29.7)	
Duration of hospitalization before COL therapy, median (min-max)	18 (3-101)	14.5 (4-52)	0.109
APACHE II (mean±SD)	25.17±6.8	21.94±7.85	**0.007**
Underlying diseases, n (%)			
COPD	61 (57.5)	25 (39.1)	**0.02**
DM	30 (28.3)	14 (21.9)	0.354
CF	24 (22.6)	9 (14.1)	0.171
CAD	30 (28.3)	10 (15.6)	0.059
Immunosuppression	7 (6.6)	7 (10.9)	0.319
Solid organ malignancy	3 (2.8)	1 (1.6)	1.0
Initial serum urea (mg/dl) median (min-max)	46 (16-125)	39.5 (9-87)	**0.02**
Initial serum creatinine (mg/dl) median (min-max)	0.8 (0.34-1.2)	0.63 (0.3-1.2)	**<0.001**
End-treatment serum urea (mg/dl) median (min-max)	116 (35-295)	43.5 (8-169)	**<0.001**
End-treatment serum creatinine (mg/dl) median (min-max)	2.46 (0.73-8)	0.72 (0.21-1.5)	**<0.001**
Concomitant nephrotoxic agent use, n (%)	78 (73.6)	34 (53.1)	**0.006**
Sulbactam	19 (17.9)	6 (9.4)	0.127
Vancomycin	14 (13.2)	8 (12.5)	0.894
NSAID	3 (2.8)	3 (4.7)	0.524
NSAID+sulbactam	1 (0.94)	1 (1.6)	0.716
NSAID+sulbactam+amikacin	2 (1.9)	1 (1.6)	0.876
ACEI+sulbactam	1 (0.94)	2 (3.1)	0.295
Aminoglycoside	1 (0.94)	1 (1.6)	0.716
ACEI+ARB	3 (2.8)	2 (3.1)	0.912
AMPHOb	1 (0.94)	1 (1.6)	0.716
Furosemide	33 (31.1)	9 (14.1)	**0.012**
Vasopressor agent use, n (%)	60 (56.6)	26 (40.6)	**0.043**
14-day mortality, n (%)	50 (47.2)	22 (34.4)	0.102
28-day mortality, n (%)	37 (34.9)	18 (28.1)	**0.029**
Overall mortality, n (%)	98 (92.5)	44 (68.8)	**<0.001**

NSAID: Non-steroidal anti-inflammatory drug, ACEI: Angiotensin converting enzyme inhibitor, ARB: Angiotensin receptor blocker, AMPHOb: Amphotericin B, min-max: Minimum-maximum, COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, CF: Cardiac failure, CAD: Coronary artery disease, COL: Colistin, SD: Standard deviation

these studies showed that nephrotoxicity frequently occurred in the first 72 hours after starting the COL[7]. In another study investigating the COL nephrotoxicity in older and younger adult patients, it was observed that the older patients had a significantly longer length of ICU stay before a COL initiation[5]. When geriatric and young patients were compared in terms

Table 2. Logistic regression analyses of risk factors for colistin nephrotoxicity

	Univariate analyses			Multivariate analyses		
	p value	Odds ratio	95% confidence interval	p value	Odds ratio	95% confidence interval
Age	**<0.001**	1.052	1.030-1.075	**0.001**	1.043	1.018-1.068
Sex (female)	0.01	0.422	0.219-0.815			
APACHE II score	**0.006**	1.064	1.017-1.112	0.435	1.022	0.967-1.080
COPD (+)	0.02	0.473	0.251-0.890			
Initial serum creatinine (mg/dl)	**<0.001**	40.320	6.389-254.465	**0.002**	23.122	3.123-171.217
Concomitant nephrotoxic agent use	**0.001**	3.057	1.598-5.849	0.02	2.398	1.147-5.012

COPD: Chronic obstructive pulmonary disease

Table 3. Nephrotoxicity based assessment in geriatric patients

Variables	Nephrotoxicity (+) n=88	Nephrotoxicity (-) n=28	p value
Sex, n (%)			0.193
Female	47 (53.4)	11 (39.3)	
Male	41 (46.6)	17 (60.7)	
APACHE II (mean±SD)	25.78±6.542	25.64±6.86	0.922
Duration of hospitalization before COL therapy, median (min-max)	18 (3-101)	14 (4-31)	0.094
Initial serum urea (mg/dl) (mean±SD)	52.42±23.01	42.18±18.59	**0.034**
Initial serum creatinine (mg/dl) median (min-max)	0.8 (0.34-1.2)	0.64 (0.3-0.95)	**0.001**
Total colistin day, median (min-max)	10 (4-23)	8.5 (4-18)	0.141
Underlying diseases, n (%)			
COPD	53 (60.2)	16 (57.1)	0.772
DM	23 (26.1)	9 (32.1)	0.536
CAD	27 (30.7)	8 (28.6)	0.832
CF	23 (26.1)	7 (25)	0.905
Immunosuppression	4 (4.5)	1 (3.6)	1
Solid organ malignancy	2 (2.3)	4 (14.3)	**0.023**
Vasopressor agent use, n (%)	33 (37.5)	10 (35.7)	0.865
Concomitant nephrotoxic agent use, n (%)	25 (28.4)	14 (50)	**0.035**
14-day mortality	46 (52.3)	14 (50)	0.865
28-day mortality	31 (73.8)	9 (64.3)	0.511
Overall mortality	84 (95.5)	23 (82.1)	**0.036**

COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, CF: Cardiac failure, CAD: Coronary artery disease, COL: Colistin, SD: Standard deviation, min-max: Minimum-maximum

Table 4. Independent risk factors associated with colistin nephrotoxicity in the geriatric patients

	Univariate analyses			Multivariate analyses		
	p value	OR	95% CI	p value	OR	95% CI
Initial serum urea (mg/dl)	**0.01**	1.021	1.005-1.038	0.493	1.007	0.988-1.026
Initial serum creatinine (mg/dl)	**<0.001**	40.320	6.389-254.465	**0.003**	22.489	2.835-178.426
Immunosuppression	0.324	1.737	0.580-5.203			
Concomitant nephrotoxic agent use	**0.001**	3.057	1.598-5.849	**0.008**	2.516	1.275-4.963

OR: Odds ratio, CI: Confidence interval

of time from the onset of COL to nephrotoxicity, there was no statistically significant difference found.

Mortality rates are higher among ICU patients due to their advanced age, disease severity, and common healthcare-associated infections. Although some studies demonstrated higher mortality in patients with a COL nephrotoxicity, others showed no difference[3,19,20]. Özkarakaş et al.[19] reported similar mortality rates between patients with and without nephrotoxicity. In another study comparing the mortality rates in older and young adult patients receiving a COL, there was no difference between the two groups found[5]. In contrast to these findings, mortality rates were statistically higher in the nephrotoxicity group and in the geriatric nephrotoxicity subgroup in our study.

The average human lifespan is increasing worldwide. According to the World Health Organization data, the older population is expected to increase from 12-22% of the total population between 2015 and 2050[21]. Age-related decline in innate immunity brings about changes in neutrophil migration, macrophage phagocytosis, and cytokine production that increases the risk of infection by extracellular pathogens[22]. Also, poorer nutrition and hygiene, organ dysfunction, reduced mucociliary activity, and comorbid conditions are other factors that increase the susceptibility to infections in older patients[1,23,24]. Most patients treated in the hospitals are the geriatric population, especially in the ICUs.

In the present study, advanced age was found to be an independent risk factor for COL nephrotoxicity. Aging affects the pharmacokinetics and pharmacodynamics of antibiotics[25]. Antibiotics reach higher concentrations in tissues with a high blood flow than in the tissues with a low blood flow, such as adipose tissue. A decrease in the serum proteins such as albumin, lean body mass, and body water, and an increase in body fat results in a reduced volume of distribution of antibiotics in older adults. Polypharmacy is common, which also increases the risk of drug-drug interactions in this patient group[26,27]. Inadequate administration of the antibiotics and failure to perform dose adjustment, and follow-up may lead to life-threatening adverse effects. All these factors increase susceptibility to infection and treatment failure in older patients, especially in the ICUs. Therefore, the dose adjustment and follow-up should be performed with consideration to the pharmacokinetic and pharmacodynamics of antibiotics.

COL is mainly excreted renally, and urinary excretion includes a renal tubular secretion. It passes through a large renal tubular reabsorption (up to 80%), and most of the filtered COL remains

Table 5. Age-based clinical and laboratory characteristics of patients with colistin nephrotoxicity

	18-64 years n=18 (16.2%)	**≥65 years n=88 (83%)**	**p value**
APACHE II (mean±SD)	22.17±7.61	25.78±6.542	**0.04**
Duration of hospitalization before COL therapy, median (min-max)	17 (5-43)	18 (3-101)	0.930
Initial serum urea (mg/dl) median (min-max)	36 (20-99)	52 (16-125)	0.081
Initial serum creatinine (mg/dl) (mean±SD)	0.74±0.191	0.78±0.204	0.424
End-treatment serum urea (mg/dl) median (min-max)	85.5 (36-266)	117.5 (43-295)	0.089
End-treatment serum creatinine (mg/dl) median (min-max)	2.34 (0.73-5.68)	2.56 (1-8)	0.970
Total colistin day, median (min-max)	14 (5-22)	10 (4-23)	0.123
Colistin toxicity day, median (min-max)	7.5 (2-19)	5 (2-18)	0.236
Underlying diseases, n (%)			
Chronic obstructive pulmonary disease	8 (44.4)	53 (60.2)	0.217
Diabetes mellitus	7 (38.9)	23 (26.1)	0.274
Coronary artery disease	3 (16.7)	27 (30.7)	0.229
Cardiac failure	1 (5.6)	23 (26.1)	0.067
Immunosuppression	5 (27.8)	2 (2.3)	**0.001**
Solid organ malignancy	0 (0.0)	3 (3.4)	1.00
Vasopressor agent use, n (%)	5 (27.8)	55 (62.5)	**0.009**
Concomitant nephrotoxic agent use, n (%)	13 (72.2)	63 (71.6)	0.957
Need for hemodialysis, n (%)	1 (5.6)	4 (4.5)	1.00
14-day mortality, n (%)	4 (22.2)	46 (52.3)	**0.02**
28-day mortality, n (%)	6 (40)	31 (73.8)	**0.019**
Overall mortality, n (%)	14 (77.8)	84 (95.5)	**0.027**

SD: Standard deviation, min-max: Minimum-maximum, COL: Colistin

in the body and is therefore mainly cleared by non-renal mechanisms. Colistin nephrotoxicity is primarily associated with d-aminobutyric acid and fatty acid components, and the mechanism of nephrotoxicity is like its antibacterial effect[28-30]. The dosing regimen of a COL should be determined considering the renal function of the patients as assessed by the creatinine clearance. Especially, care should be exercised in patients with the initial serum creatinine levels close to the upper limit, and another treatment option other than a COL should be considered in geriatric patients.

The limitations of our study are its retrospective-single-center design, the small sample size, and inability to measure a serum COL level. In this context, our data should be supported with larger sample sizes and prospectively designed studies.

Conclusion

Advanced age was found to be an independent risk factor for a COL nephrotoxicity. Close monitoring of the serum creatinine concentrations and signs of hypovolemia and hypotension of all the patients receiving a COL treatment is required. If signs and symptoms of renal failure are detected, it is recommended to continue with the required dose adjustment. Caution should be exercised especially in the geriatric patients who have initial serum creatinine levels close to the upper limit or who use concomitant nephrotoxic drugs, and if possible, another treatment option other than a COL should be considered in these patients.

Ethics

Ethics Committee Approval: The study were approved by the Niğde Ömer Halisdemir University of Local Ethics Committee (protocol number: 2018/13-21, date: 31.10.2018).

Informed Consent: Retrospective study.

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Authorship Contributions

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