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Assessment of Renal Damage in Patients with Multi-Drug Resistant Strains of Pneumonia Treated with Colistin

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Abstract

Background: Treatment of multi-drug-resistant strains of pneumonia with common antibiotics in renal patients is ineffective and physicians are compelled to use Colistin for such cases.
Objectives: This study was conducted to assess the mortality, length of stay, and renal damages in the treatment of multi-drug-resistant pneumonia with Colistin among multiple trauma patients admitted to the emergency department and transferred to the ICU.
Methods: This retrospective cohort study was conducted between 2011 and 2016. 102 multiple trauma (MT) patients with multi-drug-resistant strains of hospital-acquired pneumonia (HAP) admitted to the emergency department then transferred to the ICU were assessed. All patients received Colistin according to their weight. Renal damage was evaluated according to the RIFLE criteria. The mortality and the length of stay were assessed. In order to statistically analyze the data, SPSS version 23 software was used to conduct t-test and chi-square test.
Results: Out of 102 patients, 55 (54%) died and 50 (49.1%) developed acute renal failure; 64 cases had no hypertension. Patients according to the RIFLE index were assessed: Risk (11.01%), Injury (14%), Failure (18%), Loss (6%), and End-stage renal disease. The prevalence and prognosis of acute kidney injury in multiple trauma patients treated with Colistin were significantly correlated with drug dosage, body mass index, and use of corticosteroids (when assessed using relevant scoring systems, $P < 0.05$).
Conclusions: The use of a scoring system in the intensive care unit, determining those patients requiring Colistin, and adjusting the dosage of this drug for treatment of MT patients with multi-drug resistant strains of HAP are vital. Creatinine levels must be carefully monitored.

Keywords: Colistin, Antibiotic Resistance, Acute Renal Injury, Intensive Care, Multi-Drug-Resistant Pneumonia

1. Background

Development of resistance to common antibiotics has particular importance in the hospital settings to prevent treatment failure (1-5). Nowadays, many types of hospital-acquired pneumonia (HAP) do not respond to common antibiotics and lead to morbidity and mortality (6-10). Pneumonia is the second common cause of hospital infection and comprises about 15% of all cases (11-14). Its highest prevalence is in the intensive care unit (1, 15-18). Multi-drug-resistant strains are one of the factors that create problems when treating HAP infections (19-22). Antibiotic resistance in HAP is an indication of administration of Colistin (23-25).

Colistin or Polymyxin B exerts its antibacterial effects by destroying the cell membrane of bacteria and increasing permeability, resulting in cell death (26-29). Colistin has high bactericidal effects on many strains that are resistant to different types of antibiotics (30-33). Its effect on pneumonia and Acinetobacter has been proven (34-36).

One report mentions that treating HAP with Colistin had only a 25% positive response, due to its low penetration in lung tissues (37). On the other hand, using high dosages has severe side effects such as renal and neurotoxic damages (38, 39). Chen and colleagues (2015) found no significant difference between mono-therapy with Colistin and a multi-drug regimen containing Colistin plus another antibiotic. They compared treatment regimens and assessed mortality, hospitalization duration, and prevalence of renal damage (40).

Koksal and colleagues (2016) investigated incidence and risk factors for renal damage caused by Colistin. Fac-

tors associated with renal damage were old age, high levels of Creatinine, diabetes, and chronic obstructive pulmonary disease (41). Binh and colleagues (2015) reported a 67.9% success rate when treating patients with Colistin. However, 21.4% of the patients experienced renal damage (42). Elefritz and colleagues showed that increasing the dosage of Colistin did not increase the treatment success rate. They also reported no renal damage caused by increased dosages. However, large-scale studies are still needed (43). Valachis and colleagues (2015) investigated the effectiveness of Colistin spray in treating pneumonia. They stated that it increases the effectiveness of treatment. These studies did not report any increase in renal damage of Colistin spray (44).

2. Objectives

This study was conducted to assess hospital outcomes of treatment of multi-drug resistant HAP using Colistin in patients admitted to the emergency department and transferred to ICU.

3. Methods

The current study was retrospective cohorts from 2011 to 2016. 102 patients with HAP with multi-drug resistance at our hospital treated with Colistin entered the study. These patients admitted to the emergency department and then transferred to ICU.

Acute kidney injury (AKI), formerly called acute renal failure (ARF), was assessed using RIFLE classification. RIFLE is an acronym for Risk, Injury, Failure, Loss, and End-stage kidney disease.

Hospitalized patients with multi-drug-resistant strains of HAP that were treated by Colistin were assessed. Patients with a history of the renal disorder or renal failure, dialysis patients, individuals with a history of Colistin sensitivity, pregnant women, and patients with incomplete records were excluded.

Data on gender, age, body mass index, history of diabetes, hypertension, Creatinine level upon admission and at the beginning of treatment, daily dose of Colistin, duration of use, septic shock, APACHE- II, and sequential organ failure assessment scores (SOFA) were recorded. Quantitative variables and standard deviation (mean $\pm$ SD) and qualitative data percentages were assessed.

To analyze quantitative and qualitative data, the t-test and chi-square test were used, respectively. Data were analyzed by SPSS version 23.

4. Results

The findings of the current study showed that among 102 patients, 64 were men and 38 were women with CPIS scores of 6 or higher and without dialysis. The highest and the lowest frequencies were in 2015 (43 patients, 42.1%) and 2012 (7 patients, 6.8%), respectively. The highest frequency was in the 50-year-old age group and the lowest was in the below 30-year-old age group; 64 cases (62%) did not have hypertension; 78 patients (76%) did not have diabetes; 55 cases (56.1%) were moribund. Patients had different levels of Colistin. Administration of 3 million units of Colistin had the highest frequency among the different doses administered. The findings also showed that most of the patients (80 cases) were administered with other antibiotics along with Colistin. Patients were categorized into 3 groups in terms of Creatinine level before giving Colistin. The group exhibiting Creatinine level less than 1 had the highest frequency (57.9%). In terms of Creatinine level at discharge from the ICU, the patients were categorized into 3 groups. The group with Creatinine level of more than 11.5 had the highest frequency (70.7%). Most of the patients (70) had a septic shock.

RIFLE (Risk, Injury, Failure, Loss, and End-stage kidney disease) is a popular ranking system; it categorizes patients with renal failure into 5 groups based on glomerular filtration and urine production. The current study investigated renal damage based on the RIFLE classification. Based on the findings, 50 patients (49.01%) had a chronic renal failure. Their RIFLE classification was calculated as follows: risk (11.01%), injury (14%), failure (18%), loss (6%), and end-stage renal disease.

Diabetes showed a significant impact on renal failure, hospital mortality, and hospitalization duration ($P < 0.05$). Creatinine level before Colistin administration had a significant impact on the prevalence of renal failure, hospital mortality, and hospitalization duration ($P < 0.05$). APACHE-II score had a significant impact on the prevalence of renal failure, hospital mortality, and hospitalization duration ($P < 0.05$). The increasing APACHE-II score increased the mentioned outcomes. Based on the findings, SOFA score also had a significant impact on renal damage, hospital mortality, and hospitalization duration ($P < 0.05$), so that increasing the SOFA score resulted in an increase in the mentioned outcomes.

5. Discussion

Using a scoring system for disease severity may be a guide for the medical staff to evaluate patient's outcomes or estimate the chance for improvement (45). These prognoses may be useful in estimating patient's physiologic in-

Table 1. Demographic Information of Patients

Variable	Groups	Frequency (%)
Sex	Male	64 (62.75)
	female	38 (37.25)
Year	2010	7 (6.8)
	2011	18 (17.6)
	2012	24 (23.4)
	2013	43 (42.1)
	2014	10 (10.1)
Age	< 30	15 (14.7)
	31 - 40	23 (22.5)
	41 - 50	26 (25.4)
	50 >	38 (37.4)
Initial Dose of Colistin	1	2 (1.5)
	1.5	2 (1.5)
	2	3 (2.9)
	3	42 (41.2)
	4	12 (11.8)
	4.5	1 (~1)
	5	1 (~1)
	6	22 (21.6)
	8	4 (3.9)
	9	10 (9.8)
Antibiotic with Colistin	Yes	80 (78)
	No	21 (21)
Creatinine before Colistin	< 1	59 (57.9)
	1 - 1.5	40 (39.2)
	1.5 >	3 (2.9)
Creatinine in discharge day	< 1	16 (15.6)
	1 - 1.5	14 (13.7)
	1.5 >	72 (70.7)
Septic Shock	Yes	70 (69)
	No	31 (30)
High blood pressure	Yes	38 (37.25)
	No	64 (62.75)
Diabetes mellitus	Yes	24 (24)
	No	78 (76)
Death	Yes	55 (54)
	No	47 (46)

stability upon admission (46). In addition, severity scoring and forecasting mortality for each patient can be performed along with clinical assessment in the ICU in order to increase chances of survival (47, 48).

Based on the findings of the current study, there was a positive significant association between APACHE-II score, renal damage, mortality, and ICU duration. Several studies have investigated the association between these criteria and outcomes in patients with different diseases, finding a significant association. Asadizandi and colleagues in a study, which estimated mortality using APACHE-II severity scoring system in patients hospitalized in the ICU, calculated the APACHE-II score for both surviving and dead patients as 13.16 and 17.15, respectively. The association was statistically significant. The mortality rate in patients with scores less than 15 was estimated to be 15%; for patients with scores from 16 to 19, it was estimated to be 36%, and finally, in patients with a score from 13 to 20, it was 100% (49). Rahimzadeh and colleagues in a study showed that this scoring system could predict mortality in ICU patients (50). These results were also similar to the findings of De Campos et al. (51) and Costa e Silva et al. (52). The reason for consistency of the results of the current study with those of other studies can be the applicability of APACHE-II criterion in different diseases, particularly in renal diseases. Using this criterion during the first days of hospitalization in the ICU can predict outcomes with a high probability and provide a useful guide for healthcare teams in providing a more efficient care.

Therefore, different outcome-predicting systems, such as APACHE, SAPS, and SOFA, are used to forecast the final outcomes of ICU patients. Using a forecasting system such as APACHE-II can lead to the prediction of patient's long-term or short-term hospitalization. Mortality among patients with chronic renal damage also can be predicted.

Calculating the SOFA score in determining mortality and prognosis in chronic renal damage was another finding of the current study. An increase in the SOFA score resulted in more severe consequences and outcomes. SOFA is a common and valid criterion in scoring disease severity. Few studies used this criterion in Iran and enough attention has not been paid to it. Based on the findings of Hosseini and Ramazani, the SOFA scoring system has a good precision in forecasting outcomes in the surgical ICU as well as in the internal ICU (53). It seems that in different hospital contexts and types of antibiotic resistance, different scoring models should be used to evaluate patients in ICU and using these models is not recommended in all settings. Evaluation of the primary situation using these systems should be determined.

The association between Colistin dose and prognosis of patients with chronic renal damage was another finding of our current study. Based on the findings of the current study, Colistin dose had a significant impact on renal

Table 2. Analytical Table for Some Main Variables Such as Creatinine Before Colistin, Underlying Diseases, APACHE, and SOFA

Variables	Groups	Acute Renal Failure		Mortality		Length of Stay, Days
		Yes (N = 50)	No (N = 52)	Yes (N = 55)	No (N = 47)	
Diabetes mellitus	Yes (N = 24)	16	8	13	11	37.67
	No (N = 78)	34	44	42	36	39.01
Statistical analysis		Chi score = 16.96, P = 0.04		Chi score = 13.1, P = 0.04		T test = 8.92, P = 0.00
APACHE-II	0 - 15 (N = 16)	4	12	5	11	35.42
	16 - 19 (N = 36)	8	28	12	24	38.55
	20 - 30 (n = 39)	28	11	30	9	38.97
	30 > (N = 11)	10	1	8	3	40.41
Statistical analysis		Chi score = 14.07, P = 0.03		Chi score = 16.69, P = 0.02		T test = 6.4, P = 0.04
Sofa	< 5 (N = 12)	2	10	3	9	37.3
	5 - 10 (N = 18)	6	12	11	7	37.84
	11 - 15 (N = 58)	32	26	37	21	38.7
	15 > (N = 14)	10	4	4	10	39.81
Statistical analysis		Chi score = 19.76, P = 0.00		Chi score = 21.2, P = 0.01		T test = 8.2, P = 0.00
Creatinine before Colistin	< 1 (N = 59)	22	37	27	32	38.5
	1 - 1.5 (N = 40)	29	11	25	15	38.69
	1.5 > (N = 3)	3	0	3	0	39.31
Statistical analysis		Chi score = 22.24, P = 0.00		Chi score = 22.7, P = 0.00		T test = 9.42, P = 0.00

damage and mortality ($P < 0.05$); but there was no significant association between dosage and hospitalization duration. Since Colistin dosage is based on the Creatinine level (i.e. with an increase in Creatinine level the dose of Colistin reduced and vice-versa), determining the impact of the dosage in chronic renal damage, mortality, and hospitalization duration is critical. The association between underlying diseases and renal chronic damages is another issue that has been investigated in different studies. Based on the findings of the current study, diabetes is directly associated with renal damage and mortality. This has been investigated in other studies. Gul and colleagues (54) and Rocco and colleagues (55) found a significant association between diabetes and renal damages in patients using Colistin; this is not consistent with the results of the current study. In the current study, 23% of the patients with chronic renal damage were diabetics, and in patients with no renal damage, it was 21%; no significant association was found. Considering the underlying diseases such as diabetes, the association with chronic renal damage may vary by lifestyle factors such as a history of nutritional regime or smoking.

5.1. Conclusion

Based on the findings of the current study, the prevalence and prognosis of chronic renal damages have a direct significant association with the type of scoring system, drug dosage, body mass index, and septic shock. These systems may be useful in prioritizing patients requiring more care. Taking the scores of these systems into account may reduce renal damage associated with Colistin use in HAP patients.

5.2. Limitations

This study was conducted only in one hospital in Tehran city, Iran. Therefore, the findings need to be interpreted and generalized by caution. More research in this area is needed before generalizing the study findings.

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Footnote

Conflicts of Interest: The authors declare no conflict of interest.

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