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Original Article

The effectiveness of colistin/levofloxacin compared to colistin/meropenem in the treatment of ventilator-associated pneumonia (VAP) caused by carbapenem-resistant *Acinetobacter baumannii*: a randomized controlled clinical trial

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Abstract

Background and purpose: The treatment of ventilator-associated pneumonia (VAP) caused by carbapenem-resistant *Acinetobacter baumannii* (CRAB) is still a great challenge. This study evaluated the effectiveness of the colistin/levofloxacin regimen compared to the usual colistin/meropenem regimen in the treatment of patients with VAP caused by CRAB.

Experimental approach: The patients with VAP were randomly assigned to experimental (n = 26) and control (n = 29) groups. The first group received IV colistin 4.5 MIU every 12 h + levofloxacin 750 mg IV daily, and the second group received IV colistin with the same dose + meropenem 1 g IV every 8 h for 10 days. The clinical (complete response, partial response, or treatment failure) and microbiological responses at the end of the intervention were recorded and compared between the two groups.

Findings/Results: The complete response rate was higher (n = 7; 35%) and the failure rate was lower (n = 4; 20%) in the experimental group than in the control group (n = 2; 8%, and n = 11; 44%, respectively), but the differences were not statistically significant. Even though the microbiological response rate was higher in the experimental group (n = 14; 70%) than in the control group (n = 12; 48%), the difference was not statistically significant. The mortality rate was 6 (23.10%) and 4 patients (13.8%) in the experimental and control groups, respectively ($P = 0.490$).

Conclusion and implication: The levofloxacin/colistin combination can be considered an alternative regimen to meropenem/colistin in the treatment of VAP caused by CRAB.

Keywords: *Acinetobacter baumannii*; Colistin; Levofloxacin; Meropenem; Ventilator-associated pneumonia.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a common hospital infection that leads to significant mortality and imposes very high costs on the treatment system (1). Patients in intensive care units (ICUs) who have been on mechanical ventilation for at least 48 h, may develop VAP (2). Gram-negative bacteria resistant to therapy have been identified as the primary pathogens of VAP in most sites in recent years.

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Among gram-negative organisms, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* show the highest resistance (3). Treatment-resistant *Acinetobacter* species are considered the important causes of increasing hospitalization, hospitalization costs, and mortality, especially in ICUs. Some species of *Acinetobacter*, especially *A. baumannii*, show resistance to a wide range of antibiotics (4). Mortality from VAP associated with *A. baumannii* ranges from 40% to 70% (5-7).

A. baumannii is one of the most important opportunistic pathogens in hospital-acquired infections, particularly in ICUs (8). In 2017, *A. baumannii* was placed on the global priority list of the world health organization (WHO) for drug-resistant bacteria to highlight the need for research development and the necessity of new antibiotics (6). *A. baumannii* is known as the most common cause of VAP (6).

The resistance of *A. baumannii* to carbapenems is increasing and it is a big challenge in the treatment of infections caused by this pathogen (9). Even cases of pan-drug-resistant *A. baumannii* have been reported (10). There are few treatment options for patients with this pathogen due to high resistance to common antibiotic agents (11). The steps adopted to address the issue of multidrug-resistant (MDR) *A. baumannii* include combination therapy and research into the synergistic effect of certain antibiotics with colistin and ampicillin/sulbactam against this microbial species. Also, it has been found that the combined use of antibiotics reduces the required antibacterial therapeutic doses that reduce the risk of side effects and drug toxicity (9,12).

Some *in vitro* studies have reported the synergistic or additive effect between levofloxacin and colistin against MDR *A. baumannii* (13-15). Therefore, it is hoped that this combination will be effective in treating infections caused by this pathogen including VAP, because despite the recent measures and advances in the treatment of VAP, this disorder is still considered an important cause of death in hospitalized patients, and the treatment of cases caused by MDR *A. baumannii* has remained a big challenge. It is preferable to carry out clinical research to investigate antibiotic combinations that have synergistic effects on this pathogen to be included in the treatment regimens for this infection to achieve a desirable result. In this regard, the present study aimed to evaluate the effectiveness of the colistin/levofloxacin combination (which is shown to be synergistic) compared to the colistin/meropenem combination (which is usually used as the current standard treatment) in the treatment of VAP caused by carbapenem-resistant *A. baumannii* (CRAB).

MATERIALS AND METHODS

From September 2020 through February 2021, the current randomized controlled clinical trial was carried out at Al-Zahra Hospital of Isfahan, affiliated with Isfahan University of Medical Sciences (IUMS), Iran. The study was approved by the ethics committee of IUMS with the Ethical code IR.MUI.RESEARCH.REC.1399.606. The study protocol was registered in the Iranian Registry of Clinical Trials (IRCT) with the code IRCT20150721023282N17.

Study population

The study population consisted of all patients with VAP caused by CRAB hospitalized in the ICUs. The convenience sampling method was applied.

The inclusion criteria were as follows: (1) age over 18 years; (2) undergoing mechanical ventilation (intubation) for more than 48 h; (3) diagnosis of VAP; (4) growth of carbapenem (meropenem)-resistant *A. baumannii* in the culture of lung secretions.

The exclusion criteria were: (1) pregnancy; (2) breastfeeding; (3) history of allergy to colistin, levofloxacin, and/or meropenem; (4) acute respiratory distress syndrome; (5) suffering from active pulmonary tuberculosis; (6) simultaneous non-pulmonary bacterial or fungal infection; (7) creatinine clearance less than 60 mL/min according to the Cockroft-Gault formula; and (8) use of any other nephrotoxic drugs (*e.g.* vancomycin, any aminoglycoside, and amphotericin B).

The diagnosis of VAP was based on new or progressive infiltration on lung imaging, plus at

least two of the following symptoms of infection: fever (temperature >38 °C), leukocytosis (white blood cell > 12000/mm^3), the occurrence of purulent sputum or increased secretions of the respiratory system with a higher need for suction, plus positive tracheal sample culture (16).

Written informed consent was obtained from the patients or their guardians (including the father, mother, or child) in the case of unconsciousness to participate in the study.

Sample size

According to the findings of a previous study (17), the sample size was estimated to be 21 individuals per group among the aforementioned population using the sample size equation below at a confidence level of 95%, an 80% test power, and based on the variance of the clinical pulmonary infection score (CPIS) values of 1.62 and 2.12 for the two treatment groups, respectively, and effect size of 1.6 obtained by the mean difference of CPIS between the two groups:

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2} = \frac{(1.65 + 0.84)^2 (1.62^2 + 2.12^2)}{(4.2 - 5.8)^2} = 21$$

Microorganism identification

Sampling was performed by aspiration of endotracheal secretions. After suctioning the patients' lung secretions, about 2-3 mL of the sample was collected in a sterile sampling container and immediately sent to the microbiology laboratory of the hospital for culture, identification of the pathogen type, and determination of its antibiotic susceptibility by disk diffusion method using clinical and laboratory standards institute (CLSI) guidelines (18). The patient was included in the research if the culture yielded carbapenem (meropenem)-resistant *A. baumannii* (detected by the meropenem disk 10 µg).

Interventions

Before conducting the study, its purpose was explained to patients or their guardians and they participated in the study if they agreed and signed the written informed consent forms. First, the diagnosis of CRAB-related VAP was confirmed, as previously described, and then the included patients were randomly and equally assigned to experimental and control groups (block randomization method by blocks of four).

The patient's demographic and clinical information, such as gender, age, hospitalization cause, underlying illnesses, blood tests, disease status or severity based on the scores of Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA), and CPIS, and serum procalcitonin (PCT) levels were gathered at the start of the trial. In the control group, meropenem 1 g as a 3-h IV infusion was administrated every 8 h (19) along with a 9 mIU loading dose of colistin by IV infusion, followed by 4.5 mIU IV infusion every 12 h for 10 days. In the experimental group, levofloxacin 750 mg as a 0.5-h IV infusion was administrated every 24 h along with the same dose of colistin as for the control group for 10 days.

Assessments and outcome variables

The scores of APACHE II, SOFA, and CPIS, and the serum PCT level were again determined and recorded at the end of the intervention. The clinical response at the end of therapy, evaluated as the primary outcome variable, was classified into three categories (20) including complete response (improvement of all clinical symptoms including fever, leukocytosis, and purulent sputum), partial response (improvement of at least two of the mentioned clinical symptoms), and failure (continuation or exacerbation of the initial symptoms). This case was evaluated by the physicians. The secondary outcome variables were: (1) microbiological response at the end of the treatment in two forms: eradication (no growth of the pathogen in lung secretion culture at the end of treatment), and failure (growth of *A. baumannii* in the culture of pulmonary secretions at the end of treatment); (2) changes in the CPIS index score at the end of treatment. This index gave scores based on the clinical, radiographic, and microbiological characteristics of patients, and estimated the severity of VAP; (3) all-cause mortality rate at the end of treatment; (4) the

incidence of acute kidney injury (AKI) at the end of treatment, considered an increase in serum creatinine of 0.3 mg/dL or more within 48 h or raise of serum creatinine to ≥ 1.5 times the baseline value during the last 7 days according to the definition of The Kidney Disease: Improving Global Outcomes (KDIGO) (21).

Statistical analysis

SPSS, version 26 (IBM Corporation), software was used for statistical analysis. Continuous quantitative variables were reported as mean ± SD and qualitative variables as frequency (percentage). Data distribution was examined by the Kolmogorov-Smirnov test. The frequency distribution of qualitative variables was compared between the two groups using the Chi-square test. To compare quantitative parameters with normal and non-normal distribution between the two groups, the independent samples t-test and Mann-Whitney U test were used, respectively. Additionally, the paired samples t-test was performed to compare the values before and after the intervention. In each analysis, the significance level was considered $P < 0.05$.

RESULTS

Patients

Over the study, 91 individuals were evaluated in terms of eligibility to participate in the study, and 58 patients were included in the study based on the inclusion and exclusion criteria and were randomly classified into experimental and control groups. In the control group, three individuals were excluded from the study due to death in the first 48 h of treatment (Fig. 1).

Table 1 presents the patients' basic demographic and clinical characteristics. As shown, there was no significant difference between the two groups in terms of any baseline variables.

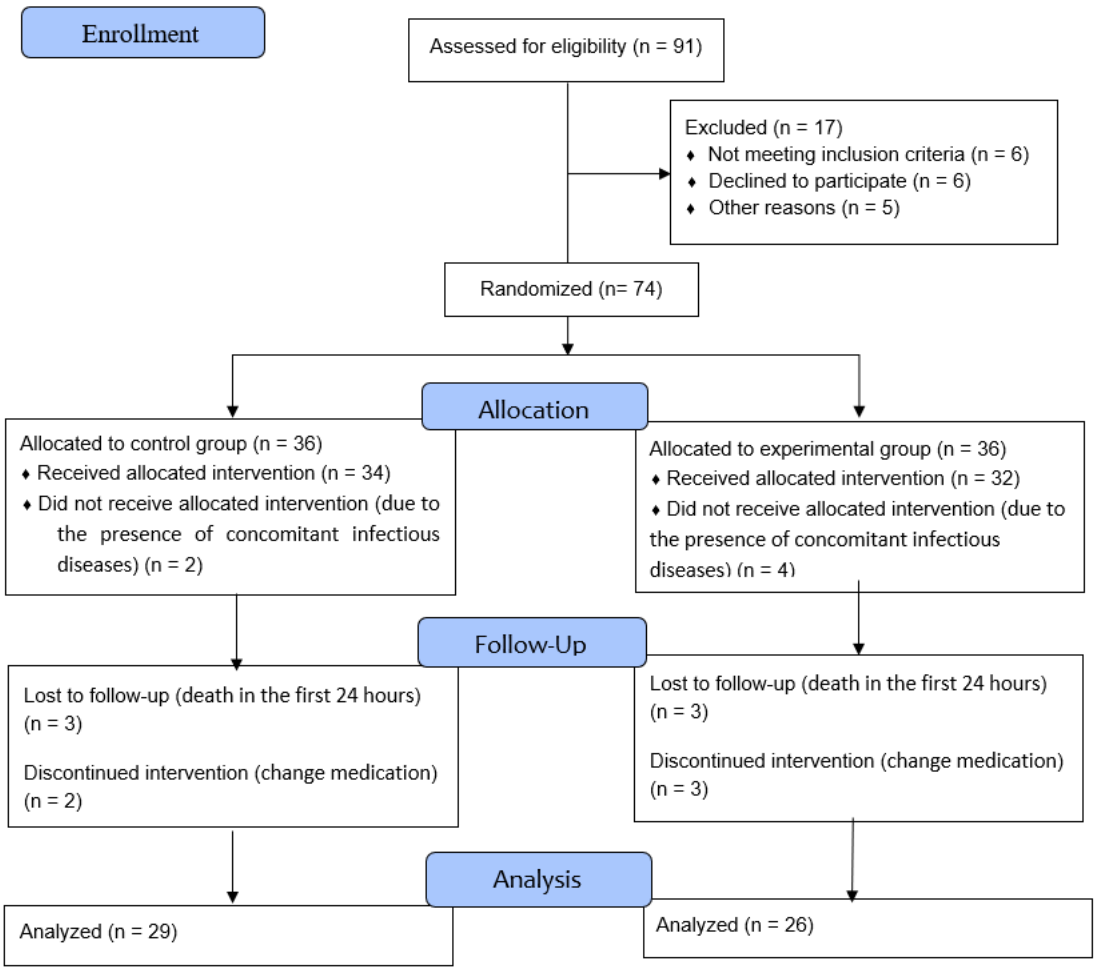

Fig. 1. CONSORT flow diagram.

Table 1. Baseline demographic and clinical characteristics of studied patients.

Parameter	Group		*P*-value
	Experimental (n = 26)	Control (n = 29)	
Age (year)	55.84 ± 20.84	55.75 ± 20.33	0.987*
Gender (n, %)			
Male	19 (73.1%)	17 (58.6%)	0.260**
Female	7 (26.9%)	12 (41.4%)	
APACHE II score	16.35 ± 4.97	18.44 ± 6.25	0.177*
SOFA score	7.57 ± 2.73	7.41 ± 2.65	0.823*
CPIS	8.76 ± 1.63	8.93 ±1.53	0.706***
WBC (cells/mm^3)	11427 ± 4806	16365 ± 25331	0.333*
Temperature (°C)	37.66 ± 0.71	37.65 ± 0.976	0.976*
Procalcitonin (mcg/L)	1.16 ± 3.50	3.24 ± 5.70	0.129***
ESR (mm/h)	54.72 ± 31.81	56.91 ± 35.71	0.821*
CRP (mg/L)	74.04 ± 31.85	86.48 ± 36.11	0.201*
Heart rate (Beats/min)	88.84 ± 15.19	102.27 ± 18.95	0.087*
MAP (mm Hg)	90.15 ± 10.45	88.00 ± 16.26	0.568*
Comorbidity			
No PMH	10 (40%)	12 (54.54%)	
IHD + HTN + HLP + DM	4 (16%)	3 (13.6%)	
DM + HTN + CVA	1 (4%)	0	
COPD	1 (4%)	1 (4.54%)	
HTN	3 (12%)	2 (9.09%)	
DM + HTN	2 (8%)	1 (4.54%)	0.662**
HTN + HLP	1 (4%)	0	
HLP	1 (4%)	0	
DM + IHD + hypothyroidism	1 (4%)	0	
Epilepsy	1 (4%)	0	
Hypothyroidism	0	1 (4.54%)	
HTN + CVA	0	1 (4.54%)	
DM + HLP	0	1 (4.54%)	
Diagnosis			
Multiple trauma	15 (57.7%)	8 (27.6%)	
COVID-19	3 (11.5%)	2 (6.9%)	
Cancer	2 (7.7%)	4 (13.8%)	
CVA	5 (19.2%)	8 (27.6%)	
Guillain-barre	1 (3.8%)	0	0.361**
Epilepsy	0	2 (6.9%)	
IHD	0	1 (3.4%)	
HSV encephalitis	0	1 (3.4%)	
PTE	0	1 (3.4%)	
Suicide	0	1 (3.4%)	
Thyroiditis	0	1 (3.4%)	

APACHE, Acute physiology and chronic health evaluation; SOFA, sequential organ failure assessment; CPIS, clinical pulmonary infection syndrome; WBC, white blood cells; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; MAP, mean arterial pressure; PMH, past medical history; IHD, ischemic heart disease; HTN, hypertension; HLP, hyperlipidemia; DM, diabetes mellitus; CVA, cerebrovascular accident; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; HSV, herpes simplex virus; PTE, pulmonary thromboembolism;*, independent-samples t-test; **Chi-square test; ***Mann-Whitney U test.

Outcome variables

Laboratory and hemodynamic indices

Table 2 compares the values of the laboratory and hemodynamic indices in the patients of the two groups. As shown, there was no significant difference between the two groups in terms of the values of these indices at the end of the study.

Disease severity indices

Table 3 presents the changes in the indices of VAP and patient status severity in each group at the end of the intervention and compares the two groups. As shown, while the CPIS score decreased in both groups at the end of the intervention, there was no statistically significant difference between the two groups. Furthermore, APACHE II and SOFA scores and PCT levels did not change significantly in the two groups at the end of the intervention, and their changes did not differ significantly between the two groups.

Table 2. Comparison of the values of the laboratory and hemodynamic parameters at the end of the study between the groups. The values are mean ± SD.

Parameter	Group		*P*-value*
	Experimental (n = 26)	Control (n = 29)	
WBC (cells/mm^3)	16292 ± 26958	11065 ± 5460	0.310
CRP (mg/dL)	74.80 ± 30.65	76.90 ± 38.16	0.840
HR (bpm)	88.85 ± 15.19	100.37 ± 24.10	0.040
MAP (mm Hg)	91.11 ± 13.80	87.79 ± 14.78	0.390
Temperature (°C)	37.18 ± 0.37	37.26 ± 0.54	0.540

WBC, White blood cells; CRP, c-reactive protein; HR, heart rate; MAP, mean arterial pressure; *, independent-samples t-test;

Table 3. The changes in outcome parameters during the study and their comparison between the groups. The values are mean ± SD.

Parameter	Time	Group		*P*-value (between-groups)
		Experimental (n = 26)	Control (n = 29)	
CPIS	Baseline	8.76 ± 1.63	8.93 ± 1.53	0.700*
	End	3.80 ± 46.2	4.36 ± 2.43	0.440*
	Difference	-4.85 ± 2.36	-4.72 ± 3.15	0.879*
	P-value (within-groups)	< 0.001**	< 0.001**	
PCT	Baseline	1.67 ± 3.50	2.83 ± 5.18	0.175*
	End	2.60 ± 8.33	1.82 ± 3.15	0.652*
	Difference	1.43 ± 7.75	-1.01 ± 5.04	0.179*
	P-value (within-groups)	0.375**	0.299**	
APPACHE II	Baseline	16.35 ± 4.97	18.44 ± 6.25	0.177*
	End	16.73 ± 10.19	17.75 ± 7.58	0.670*
	Difference	0.38 ± 9.02	-0.58 ± 5.22	0.980***
	P-value (within-groups)	0.830**	0.486**	
SOFA	Baseline	7.57 ± 2.73	7.41 ± 2.65	0.823*
	End	8 ± 3.79	7.48 ± 2.73	0.560*
	Difference	0.42 ± 2.26	0.068 ± 3.67	0.227***
	P-value (within-groups)	0.350**	0.920**	

CPIS, Clinical pulmonary infection score; PCT, procalcitonin.; APACHE, acute physiology and chronic health evaluation; SOFA, sequential organ failure assessment; *, independent-samples t-test; **, paired-samples t-test; ***Mann-Whitney U test.

Table 4. The rate of each type of clinical response in study patients and their comparison between the groups. The values are frequency and percentages.

Groups	Clinical response			*P*-value*
	Complete	Partial	Failure	
Experimental	7 (35%)	9 (45%)	4 (20%)	0.050
Control	2 (8%)	12 (48%)	11 (44%)	
***P*-value**	0.057	0.841	0.090	
OR (95% CI)	4.375 (1.019-18.788)	0.938 (0.498-1.766)	0.455 (0.170-1.213)	

*Chi-square test.

Clinical and microbiological responses

Table 4 presents the type of clinical response rate in the study groups and compares them in this regard. As shown, even though the rates of complete response and treatment failure in the experimental group were, respectively, higher and lower than in the control group, the differences were not statistically significant between the two groups. Moreover, although the microbiological response rate in the experimental group (n = 14; 70%) was more than in the control group (n = 12; 48%) at the end of the intervention, the difference was not statistically significant (*P* = 0.138).

Mortality rate

The all-cause mortality rate was 6 patients (23.10%) in the experimental group and 4 patients (13.8%) in the control group during the intervention; however, the difference was not statistically significant (*P* = 0.490; OR: 1.673, 95% CI: 0.530-5.279).

Nephrotoxicity rate

The incidence of AKI was 10 cases (40%) in the experimental group and 7 (24.10%) in the control group during the intervention; however, the difference was not statistically significant (P = 0.211; OR: 1.657, 95% CI: 0.741-3.704).

DISCUSSION

The present study was conducted to investigate the effectiveness of the colistin/levofloxacin combination compared to the colistin/meropenem combination in the treatment of VAP caused by carbapenem-resistant *A. baumannii* in 55 patients. The two research groups were identical in terms of basic demographic and clinical characteristics at the beginning of the study.

The patients' clinical responses indicated that a higher percentage of patients responded completely to the treatment in the colistin/levofloxacin group, and the rate of treatment failure was higher in the colistin/meropenem group. The colistin/levofloxacin regimen may have been superior, even though the differences were not statistically significant, according to the apparent difference in the ratios and the proximity of the *P*-value to the significant limit. Probably a larger sample size could shed much light on the difference. Furthermore, 70% of patients in the colistin/levofloxacin group and 48% of the patients in the colistin/meropenem showed microbiological responses to the treatment. Despite the lack of statistically significant difference, it seems that the success of the test combination was greater in removing the pathogen (CRAB) that could contribute to the higher rate of complete clinical response. The effect might be due to the synergistic effect between levofloxacin and colistin. Wei *et al.* reported the synergistic effects of the levofloxacin/colistin combination against clinical isolates of MDR *Acinetobacter*. This study indicated the effect of this combination against the biofilm that contains these strains (13). Since the biofilm formation contributes to the pathogenesis of VAP and its resistance to treatment (due to insufficient penetration of antibiotics and the lack of host defense mechanisms) (22), this effect can also be involved in the effect of the colistin/levofloxacin regimen.

In a laboratory study, Safarika *et al*. demonstrated that the levofloxacin/colistin combination had a synergistic effect on 90.9% of *P. aeruginosa* and 84.8% of *A. baumannii* isolates obtained from patients with VAP at the first four hours after growth. In the first four days after growth, the combination of levofloxacin and imipenem had a synergistic effect on 55.3% of *P. aeruginosa* isolates, but the synergistic effect of the colistin/imipenem combination was minimum inhibitory concentration (MIC)-dependent. According to the research, levofloxacin may be utilized to treat resistant infections brought on by these bacteria (14). Based on our research, this is the first clinical study on the comparison of the effectiveness of colistin/levofloxacin combination with colistin/meropenem combination, and only one clinical study compared the effectiveness of this combination with the levofloxacin/ampicillin/sulbactam regimen. Mosaed *et al*. studied the safety and effectiveness of the levofloxacin/colistin combination compared to the combination of levofloxacin with a high dose of ampicillin/sulbactam in treating patients with VAP caused by MDR *Acinetobacter* and reported that the combination of levofloxacin (intravenous 750 mg daily) with high-dose ampicillin/sulbactam (24 g per day) as a continuous infusion was associated with greater effectiveness and lower risk of nephrotoxicity than the levofloxacin/colistin combination in patients with MDR *Acinetobacter* VAP (17). Therefore, consistent with our results, this study shows potentiating effect of levofloxacin with another antibiotic for the treatment of this infection.

In a retrospective study on the effectiveness of four combined drug regimens in the treatment of VAP caused by resistant *Acinetobacter*, the levofloxacin/sulbactam combination led to improvement in 71.4% of cases, while levofloxacin/meropenem combination caused improvement in 63.6% of cases. Among the regimens, there were no discernible differences in the improvement rates (23). The rates of desirable clinical response with levofloxacin-containing

regimens in this study are somewhat similar to our results (80% overall improvement rate). A laboratory study examined the effect of levofloxacin in combination with ampicillin/sulbactam and tigecycline against resistant strains of *Acinetobacter* and it was reported that levofloxacin with ampicillin/sulbactam had a synergistic effect on 90% of isolates, while the combination of ampicillin/sulbactam and tigecycline did not have any significant synergistic effect (24). Even though the two aforementioned studies did not use colistin as a combination drug, the potential of levofloxacin to improve the clinical response of VAP is consistent with the present study. Furthermore, an *in vitro* study by Kheshti *et al*. reported that the combination of colistin with each of the six antibiotics including ciprofloxacin, levofloxacin, imipenem, meropenem, ampicillin/sulbactam, and rifampin had a synergistic effect against *A. baumannii* strains (25). Therefore, the acceptable response, observed in the present study, could be due to the synergistic effect of both evaluated regimens against CRAB.

In this study, the rate of nephrotoxicity was more common in the colistin/levofloxacin group than in the colistin/meropenem group. Although the difference was not statistically significant, this finding might serve as a caution about the potential drawbacks of this regimen (colistin/levofloxacin). However, as some of our study patients might suffer from sepsis following VAP during the intervention, the AKI rate might have been affected by this factor. Thus, the risk of nephrotoxicity should be researched in future trials with a larger sample size. Consistent with our result, the incidence of AKI in the study of Mosaed *et al*. mentioned previously, was considerably lower in the ampicillin/sulbactam group than in the colistin/levofloxacin group (17). Nephrotoxicity is not a common side effect of fluoroquinolones, but there are some case reports of this complication (26). A case-control study reported a slight significant increase in the risk of AKI in men who consumed oral fluoroquinolones, and the risk increased with the simultaneous use of these drugs with renin-angiotensin system inhibitors (27). Therefore, the combination of levofloxacin with other nephrotoxic drugs (*e.g.* colistin) may be associated with a higher risk of kidney injury.

Although this study evaluated APACHE II and SOFA indices, the evaluation of changes in these parameters was only a secondary goal of the study because these indices are not useful for determining the type of treatment and evaluation of the treatment outcomes. APACHE II index helps determine the risk of death, and the SOFA score only helps identify patients who have a high risk of death due to infection. To be sure that the patients in the two groups had the same mortality risk, these two indices were determined. As seen, the scores for both criteria were statistically equal between the two groups at the start of the study, suggesting that the patients in the two groups had similar levels of organ involvement and critical condition severity at baseline. The lack of significant difference in the scores of the two indices between the two groups at the end of the intervention indicated that the status remained the same during the study and the interventions did not affect the determinants of these indices.

The main limitations of the present study were small sample size, lack of placebo (open-label design), lack of MIC determination for the tested antibiotics, and no exclusion of patients with possible sepsis which may affect the evaluated outcome variables. Furthermore, the use of low-dose meropenem could be another limitation of this study; because, currently, high-dose extended-infusion meropenem has been considered a component of combination therapy for the treatment of moderate to severe CRAB infections (28). Therefore, future trials with high-dose meropenem (*i.e.* 2 to 3 g every 8 h) are suggested in this regard.

CONCLUSION

According to the results of the current study, both colistin/levofloxacin and colistin/meropenem combinations had the same effects on the clinical and microbiological improvement of VAP. Even though the key outcome factors in the current study did not significantly vary between the two regimens,

the rates of full clinical and microbiological responses were greater in the levofloxacin-containing group. Compared to levofloxacin, meropenem is more expensive and its frequent use could lead to high drug resistance. Regarding the disadvantages caused by the overuse of meropenem and its occasional shortages in the pharmaceutical market and the same effectiveness of the two tested regimens, it is possible to consider levofloxacin/colistin combination an alternative regimen to meropenem/colistin in the treatment of VAP caused by carbapenem-resistant *A. baumannii*.

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Conflict of interest statement

The authors declared no conflicts of interest in this study.

Authors' contribution

M. Momenzadeh was the principal investigator of the study. R. Soltani participated in preparing the concept and design. M. Momenzadeh, R. Soltani, F. Shafiee, A. Hakamifard, M. Pourahmad and S. Abbasi reviewed the manuscript and critically evaluated the intellectual contents. All authors participated in revising the manuscript and preparing the final draft of the manuscript. All authors have read and approved the content of the finalized manuscript and confirmed the accuracy and integrity of any part of the work.

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