Intravenous colistin is increasingly used to treat multidrug-resistant Gram-negative infections. Highly variable nephrotoxicity rates were reported by recent studies. Recent PK/PD studies propose a loading dose and a maintenance dose calculation for better efficacy and safety and for renal toxicity of such regimens. This study aimed to evaluate incidence and risk factors for nephrotoxicity associated with colistin, after implementation of a new dosing regimen including a loading dose.

### Materials & Methods

A prospective observational study was conducted among adult patients who received intravenous CMS treatment for 3 to 7 days at a West Coast University Hospital. The patients receiving intravenous CMS treatment for 48 h as part of their standard care due to the presence of a probable or a documented infection caused by multidrug-resistant pathogens. They were <18 years of age, received intravenous CMS treatment for <48 h, or had a need for hemodialysis after their course of therapy. If a patient received multiple courses of therapy, only the first one was included in the analysis. All patients received intravenous colistin sulfate (Columycin®). Rosmapa Pharma – Turkey) administered intravenously over 30 min. Each vial contained 150 mg of colistin base activity (CBA).

The following clinical data were collected: age, gender, body weight, Acute Physiology and Chronic Health Evaluation (APACHE) II score (in the first 48 h), comorbidities (diabetes mellitus, chronic renal failure, coronary heart disease, immunosuppression), type of infection, daily doses and duration of colistin therapy, concomitant antibiotics, concomitant nephrotoxic agents (including aminoglycosides, vancomycin, nonsteroidal anti-inflammatory drugs, intravenous radiocontrast agent, diuretics, dehydrating agent, clinical and microbiological responses to therapy. Renal function was assessed as calculated serum creatinine.

### Results

Fifty-nine patients met the inclusion criteria, and 31 (52.5%) developed nephrotoxicity. The APACHE-II score at colistin initiation was >15 in 81% of patients. All patients had microbiologically documented nosocomial pneumonia and/or bacteremia, soft tissue infections or central venous catheter-related infections caused by multidrug-resistant Gram-negative bacteria. The number of days that estimated target plasma concentrations of colistin were <3.5 mg/L in the first week of therapy was 10 (range: 0-30) days. The number of days that estimated target plasma concentrations of colistin were ≥3.5 mg/L in the first week of therapy was 1.94±2.24 (1.00) days. The number of days that estimated target plasma concentrations of colistin were ≥3.5 mg/L in the first week of therapy was 1.94±2.24 (1.00) days. Nineteen patients received the loading dose of 300 mg iv, followed by a maintenance dose every 8 to 12 h based on serum levels. The following clinical data were collected: age, gender, body weight, Acute Physiology and Chronic Health Evaluation (APACHE) II score (in the first 48 h), comorbidities (diabetes mellitus, chronic renal failure, coronary heart disease, immunosuppression), type of infection, daily doses and duration of colistin therapy, concomitant antibiotics, concomitant nephrotoxic agents (including aminoglycosides, vancomycin, nonsteroidal anti-inflammatory drugs, intravenous radiocontrast agent, diuretics, dehydrating agent, clinical and microbiological responses to therapy. Renal function was assessed as calculated serum creatinine.

### Conclusion

In this cohort of severely ill ICU patients, colistin led to a relatively high rate of nephrotoxicity (52.5%). Further studies are needed to identify the optimal dose for both efficacy and safety. Monitoring colistin plasma concentrations may be a useful strategy for prevention of AKI.