# *Intravenous Colistin Use in Children: Single-Center Experience*

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**Abstract**

**Objective:** Colistin, a bactericidal antibiotic, was used in the 1960s for the treatment of infections by gram-negative bacteria. Because of its side effects and the development of safer drugs, its use was abandoned in the 1980s. In infections within clinics where multi-drug-resistant gram-negative bacteria (MDRGNB) (especially *Pseudomonas spp.* and *Acinetobacter spp.*) are present, colistin usage is suggested if there is drug resistance to any other antibiotics. Nephrotoxicity is one of the commonly observed adverse effects following intravenous (IV) administration of colistin. Nephrotoxicity is dose-dependent and reversible. The aim of this study is to evaluate the efficacy and safety of colistin in MDRGNB infections occurring in pediatric and neonatal patients.

**Material and Methods:** The files of all patients under the age of 18 who were given IV colistin treatment, apart from inhaler treatments, were retrospectively investigated. Demographic characteristics of patients, risk factors for systemic infection, causative microorganisms, and susceptibilities and side effects of colistin were evaluated.

**Results:** Twenty-three patients meeting the criteria were included in the study. The median age was 2 years (4 days-17 years). Colistin was used for infections caused by MDR Acinetobacter baumannii 78.2% (18/23) and MDR *Pseudomonas aeruginosa* 21.8% (5/23). MDR *A. baumannii* was found growing in the blood cultures of 15 patients and in the urine, wound, and respiratory sample of 1 patient. MDR *P. aeruginosa* was found in respiratory samples of 4 patients and the blood culture of 1 patient. The duration of treatment with colistin was a median of 13 (4-30) days. All patients were given additional antibiotics with colistin. The most commonly used antibiotics were carbapenems (13 patients), with 5 patients given sulbactam-ampicillin, 4 given ciprofloxacin, and 3 given aminoglycoside. One patient died during treatment with colistin. No patient developed nephrotoxicity or neurotoxicity.

**Conclusion:** It appears that IV colistin use is effective and safe for MDRGNB treatment in pediatric patients.
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**Keywords:** Colistin, gram-negative bacterial infections, hospital infections, antibiotic resistance

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## Introduction

Multi-drug resistant gram-negative bacteria (MDRGNB) are defined as intrinsically a resistance ofa bacteria against at least three different antibiotic groups such as beta-lactams, aminoglycosides, quinolons andcarbapenems. Nosocomial multi-drug resistant (MDR) microorganisms are prevalent all over the world and their incidence has been gradually increasing (1, 2). Therefore, there have been efforts in search for new drugs in order to be able to combat against these organisms (3). The use of colistin, which is an old drug, but avoided due to its possible side effects has been increasingly rising due to its bactericidal efficiency (4-6). There have been many current studies regarding the systemic use of colistin in adults (7, 8). Studies investigating the efficiency and reliability of colistin in children have been gradually increasing as well. In this study, the efficiency and reliability of colistin in children was evaluated.

## Material and Methods

This study was carried out retrospectively. It included children who were given colistin against MDRGNB and hospitalized mostly in the pediat-

ric intensive care unit and pediatric surgery intensive care units together with neonatal intensive care unit, pediatric services and other surgery services of Medical School at Marmara University. Patients who had MDR *Acinetobacter baumanii* and *Pseudomonas aeuroginos* in their blood, endotracheal aspirate, wound site swab, urine and phlegm cultures, and were treated with systemic colistin between January 2011 and January 2013 were included in the study. The patients using colisin less than three days were excluded from the study. Demographic data (age, gender etc.) of the patients, medical histories (risk factors for the systemic infection, comorbidity), central venous catheter usage (CVC), the presence of medical devices such as foley catheter, endotracheal tube, tracheostomy tube, the drugs used with or before colistin. The type of the causative microorganism and its antimicrobial sensitivity, route of colistin usage, dosage, side effects of colistin, treatment results of antimicrobial therapy and prognosis were all recorded down. Urea, keratin, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and hematologicvalues of the patients were monitored.

Nosocomial multi-drug resistant (MDR) was considered to be resistant against at least three antibiotic groups. The definition of nosocomial infection was made in accordance with the criteria of Centers for Disease Control and Prevention (CDC) (9). Clinical course was decided based onthe improvement in the clinic and laboratory results and bacteriologic response of the patient. Clinical response was decided based on total improvement in the clinic results of the infection at the end of colistin therapy. Clinical non-response, on the other hand, was decided based on whether the early symptoms continued, getting worse even more a positivity or the development of a new infection. Bacteriologic response was decided based on whether there was growth in the control cultures, and non-response if culture positivity persisted. Microbiologic sensitivity was interpreted based on the definition guide of the Clinical and Laboratory Standards Institute (10).

Renal failure was decided based on the increase of the keratin over the values in line with the age of the patient. The patient was followed up with regards to other causes that might lead to renal failure. The neurologic side effects (neuromuscular blockage, changes in consciousness, attacks, vertigo, muscle weakness and apnea) likely to emerge during colistin therapy were recorded down.

VITEK 2 automatized systems were used for the identification of GNBs and antimicrobial sensitivity (bioMerieux, Marcy l'Etoile, France). Colistin sensitivity was investigated by the E-test.

## Statistical analysis

For descriptive statistics and analyses, Statistical Package for the Social Sciences (SPSS) (Release 16.0; SPSS Inc. Chicago, Illinois, USA) program was used. Whether the data had normal distribution was evaluated by the Shapiro-Wilk normality test. The variables distributed normally were given as average and standard values, and those not distributed normally with median values (minimum-maximum).

## Results

Twenty-three patients given colistin therapy between January 2011 and January 2013 were evaluated. There was no patient with two-time colistin use episode. All the patients were given colistimethate sodium (1 mg colistin=12,500 IU) intravenously (IV).

Drug dose was calculated in accordance with the body weight and creatinine clearance of the patients. All the patients were given the colistin therapy after the culture antibiogram results were obtained. Twenty patients received the antimicrobial treatment before colisten therapy. Eighteen of the twenty patients received carbapenemtherapy before the colistin therapy. Thirteen (56.5%) of the patients were male and ten were (43.5%) female. The median age of the patients was two (4 days-17 years) years. Median value of colistin therapy period was 13 (4-30) days. Median value of the hospital-stay duration of the patients before the onset of colistin therapy was 20 (0-90) days. Three patients were transferred to our hospital from other medical centers and their colistin therapys were started. The average urea values before and after treatments were; 14.6±6.1 and 14.2±4.8 mg/dL, average creatinine values before and after treatment were 0.47±0.27 and 0.45±0.25 mg/dL resoectively. Colistin was used 78.2% (18/23) in MDR*A. baumanii* 21.8% (5/23), in MDR *P. aeuroginosa* infections. Both *A. baumanii* and *P. aeuroginosa* infections were only colistin-sensitive. MDR *A. baumanii isolated* in blood culture in 15 patients, in urineculture, scar and respiration samples in each one. MDR*P. aeuroginosa*, on the other hand, grew respiration samples in four patients and in blood culture in one patient (Table 1). All the patients were given an extra antibiotic in addition to colistin. While the most used antibiotic was carbapenems (13 patients), in descending order 5 patients were given ampicillin-sulbactam, four patients ciprofloxacin and three patients aminoglycoside treatments (Table 2). Two of these patients received colistin, ciprofloxacin and amicasin therapy and one patient received colistin, imipenem and amicasin therapy. Ten patients received various nephrotoxic drugs such as aminoglycoside, vancomycin, ciprofloxacin and radiocontrast

matter (Table 2). A four-day old patient with duodenal atre- sia and situs inversus totalis received vancomycin, amicasin and ciprofloxacin together with colistin. No antibiotic-related side effect was observed in this patient who was treated for fourteen days. However, the patient died in another infection attack.

The most common underlying diseases in patients with MDRGNB growth were chronic neurologic diseases (60.8%). The other predisposing factors are congenital heart disease, surgical practices, prematurity, immune suppressive therapy, chronic lung disease, chronic renal failure, malignity, nephrotic syndrome and Down syndrome (Table 1).

**Table 1.** Clinical characteristics, microbiologic findings and demographic data of MDRGNB*-caused nosocomial infections

| | |
|---|---|
| **Age [median (min-max)]** | **2 (4 days-17 years)** |
| **Patient under three [n (%)]** | **13 (56,5)** |
| **Male [n (%)]** | **10 (43.4)** |
| **Underlying disease [n (%)]** | **22 (95.6)** |
| Chronic neurologic and neuromuscular disease | 14 (60,8) |
| Congenital heart disease+prematurity+ chronic lung disease | 1 (4.3) |
| Malignity | 1 (4.3) |
| Surgery | 1 (4.3) |
| Prematurity | 1 (4.3) |
| Down syndrome | 1 (4.3) |
| Immunosuppressive therapy | 1 (4.3) |
| Chronic renal failure | 1 (4.3) |
| Nephriticsyndrome | 1 (4.3) |
| **Mechanic ventilation [n (%)]** | **7 (30.4)** |
| **Mechanic ventilation period [median (min-max)]** | **20 (2-75)** |
| **Hospital-stay period before infection [median (min-max)]** | **20 (0-90)** |
| **Invasivetool use [n (%)]** | |
| Tracheostomy | 7 (30.4) |
| Centralvenous or arterialcatheter | 5 (21.7) |
| Endotracheal tube | 4 (17.3) |
| **Microorganism [n (%)]** | |
| *Acinetobacter baumannii* | 18 (78.2) |
| *Pseudomonas aeruginosa* | 5 (17.8) |
| **Isolation site of microorganism [n (%)]** | |
| Blood | 16 (69.5) |
| Respiration sample | 5 (21.7) |
| Urine | 1 (4.3) |
| Wound swab | 1 (4.3) |

*MDRGNB: multi-drug resistant gram-negative bacteria; **CRF: chronic renal failure

Colistin was used for bloodstream, urinary system and decubitus ulcer infections (Table 2).

Colistin was given to all patients intravenously (IV). None of the patients were given intraventricular and/or intrathecal colistin. Only the patients given inhaler colistin were excluded from the study. It was given 7.5 mg/kg/day three doses to a patient with cystic fibrosis and 1.5/mg/kg/36 hour dose to a patient with renal failure. Except these two patients, all the rest of the patients were given 5 mg/kg/day three doses.

There was no impairment in the kidney function tests of any of the patients during colistin use. No neurologic

**Table 2.** Characteristics of nosocomial infectionsand results of colistin therapy

| **Therapy indications** | **[n (%)]** |
|---|---|
| BSI** | 16 (69.5) |
| Pneumonia | 3 (13) |
| VAP* | 2 (8.6) |
| Urinarysystem infection | 1 (4.3) |
| Decubitusulcer infection | 1 (4.3) |
| **Antibiotics used together with colistin [n (%)]** | |
| Carbapenems | 13 (56.5) |
| Sulbactam-ampicillin | 5 (21.7) |
| Vancomycin | 4 (17.3) |
| Fluoroquinolones | 4 (17.3) |
| Aminoglycosides | 3 (13) |
| Linezolid | 1 (4.3) |
| **Therapy period [(median) (min-max)]** | **13 (4-30)** |
| **Side effects of colistin** | **3 (13)** |
| Elevated liver enzymes (temporary) | 2 (8.6) |
| Diarrhea | 1 (4.3) |
| Neurologic | 0 (0) |
| Kidney | 0 (0) |
| **Neurologic disease, sedation and analgesicuse [n (%)]** | **14 (60.8)** |
| **Accompanying nephrotoxicdrug use [n (%)]** | |
| Fluoroquinolones | 4 (17.3) |
| Vancomycin | 4 (17.3) |
| Aminoglikozid | 3 (13) |
| Radiocontrast agents | 1 (4.3) |
| **Therapy results [n (%)]** | |
| Microbiologic response | 23 (100) |
| Clinic response | 22 (95.6) |
| Mortality | 1 (4.3) |
| Discontinuation of therapy due to side effects | 0 (0) |
| Therapy change due to clinic non-response | 0 (0) |

VAP: ventilator-associated pneumonia BSI: blood stream infections

side effect (attack, changes in consciousness, vertigo, muscle weakness, neuromuscular blockage and apnea), electrolyte disorder or cytopenia developed in any of the patients in our study. Mild elevated liver enzymes occurred only in two patients. While one of these patients received colistin simultaneously with ampicillin-sulbactam, the other patient simultaneously received imipenem therapy. Both of the patients had un-diagnosed neuromuscular diseases. When the treatment of these patients discontinued, liver enzymes were normalized again.

During the colistin therapy, diarrhea developed in one patient. *Clostridium difficile* test toxin in stool three times, parasite, ameba and giardia antigen, adenovirus, rotavirus antigen were negative. Stool culture was negative. This patient simultaneously received ciprofloxacin together with colistin. At the end of the therapy, diarrhea recovered.

One patient died during the treatment. This case was a patient with a 30-week premature birth history, and was monitored for nearly 75 days on a ventilator, had congenital diaphragmatic hernia, lung hypoplasia and truncus arteriosus. This patient had MDR *A. baumannii*-related bloodstream infection. It was on the 24$^{th}$ day of colistin therapy. Before the colistin therapy started, the patient received imipenem therapy for 33 days and vancomycin therapy for 39 days. For this patient, it was not possible to differentiate whether the reason exitus was primary diseases or an infection.

No resistance against colistin was found in any of the patients.

## Discussion

The emergence of nosocomial MDRGNB has increased the interest in colistin which has a quick bactericidal effect to GNBs (4). Colisitn is effective almost in all *P. aeruginosa, Acinetobacter* and *Klebsiella* spp. (11). In this study, we investigated IV colistin use in 23 patients with nosocomial MDRGNB infection. Although we had limited number of patients, we found that colistin was effective and reliable against life-threatening MDRGNBs.

While clinical success rate in previous adult studies examining colistin use was 57-100%, mortality rates varied 0-62% (12). In their study they carried out in third level intensive care units in Turkey, Karbuz et al. (12*)* reported that clinical success rate was 73.7% and infection-related mortality was 15.7%. In this study we found that mortality rate was 4.3%. However, when patient groups were examined, it was revealed that all the patients in Karbuz et al.'s (12) study were critical inpatients in the third level intensive care units and they had many accompanying comorbid factors. Most of the exitus patients were composed of ventilator-associated pneumonia (VAP) and bacteremia. Although most of our cases were composed of intensive care unit patients, there were also clinic patients who did not need intensive care. Furthermore, the number of our patients was less than that of Karbuz et al. (12) Because of all these reasons, we are of the opinion that an infection-related mortality rate in our study is lower that Kabuz et al.'s (12) study.

In a study that investigated IV colistin use in children, no side effect was observed despite long-term of 40, 42, 46, 51, 70 and 93 days and high dose colistin use (13). The longest period of colistin use in our study was 30 days and standard dose therapy was given. No side effect was observed in patients with these doses.

It was reported in previous pediatric studies that the success rate of colistin therapy in MDRGNB infections was 70-86% (1, 4, 6, 12). While the our success rate was microbiologically 100% in this study, survival rate was 95.6%.

Even though colistin could be used in a combined way in clinical practice as it as the case in our study, clinic studies failed to prove that combine use was superior to single use (14-16). Besides, it was proved that in *A. baumannii, P. aeruginosa* and *K. pneumoniae* infections, colistin had in vitro synergy effects together with especially aminoglycosides, carbapenems and rifampicin (16-18).

In pediatric studies, the dose was reported as 1.3-5 mg/kg/day 2-4 doses (1, 13, 19-21). The maximum dose of colistin, on the other hand, was reported as 7.5 mg/kg/day (13). Except the two patients with cystic fibrosis and renal failure in our study, we implemented 5 mg/kg/day 3 doses therapy.

It can develop resistance to colistin during the treatment (13). Resistance development is associated with long-term use of colistin, especially to do with the fact that colistin fail to reach high tissue concentration in ventriculitis and pneumonia infections. (13). In our patients, on the other hand, no resistance was found against colistin during the treatment.

Colistin use-related nephrotoxicity incidence varies between 0 and 14.3% (22). Nephrotoxicity emerges especially with the simultaneous use of nephrotoxic drugs such as aminoglycoside (13, 17, 18). In recent studies, nephrotoxicity was found as 2.3% (14). In third level intensive care units in Turkey, in a study in which systemic colistin use was investigated in 38 episodes in 29 patients, it was found that nephrotoxicity developed only in one patient. However, the study failed to prove convincingly that nephrotoxicity was related to colistin (12). Nephrotoxicitywas found to be associated with cumulative dose (22). However, nephrotoxicity and colistin were not found to be related with colistin serum concentration (23). Therefore, serum level of colistin is not recommended to be monitored routinely.

Colistin-related nephrotoxicity usually has a mild course and returns to normal when the drug is discontin-

ued (1, 4, 7, 24, 25). In our study, despite the presence simultaneously-used cases together with nephrotoxic agents such as aminoglycoside, vancomycin and radiocontrast matter, no nephrotoxicity was found in any of the patients. Even though the number of cases was low, this study demonstrated that colistin toxicity was less than it was thought to be.

In previous studies, colistin neurotoxicity was reported to be frequent (26). In recent studies, either very little or no colistin nephrotoxicity was found (1, 4, 7, 12, 13, 21). In our study, on the other hand, no neurotoxicity was found in any of the patients. While this particular situation may be related to non-development of colistin-related neurotoxicity, it may also be related to the fact that the study is a retrospective one and that these patients had taken sedoanalgesia.

The limitation of our study is that it is a retrospective one. Another disadvantage is that the number of patients was low and the age group was heterogeneous. The other therapies taken by the patients and the sedoanalgesias have especially made the evaluation of neurologic side effects complicated. Moreover, the fact that the patients received other drugs in addition to colistine prevented the evaluation of colistine effects alone failed to allow colistin to be evaluated alone.

## Conclusion

Our study demonstrated that colistin was tolerated well by children in every age group. Given the severity and mortality of the diseases, the side effects are at an acceptable level. Colistin is very effective and reliable in MDRGNB-caused infections. Since colistin is one of the "last resort" drugs for MDRGNB-caused infections, its rational use is crucially important.

**Ethics Committee Approval:** Ethics committee approval was not received due to the retrospective nature of this study.

**Informed Consent:** Written informed consent was not obtained due to the retrospective nature of this study.

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## References

1. Goverman J, Weber JM, Keaney TJ, Sheridan RL. Intravenous colistin for the treatment of multi drug resistant, gram-negative infection in the pediatric burn population. J Burn Care Res 2007; 28: 421-6. [CrossRef]
2. Souli M, Galani I, Giamarellou H. Emergence of extensively drug-resistant and pandrug-resistant Gram-negative bacilli in Europe. Euro Surveill 2008; 13.
3. Boucher HW, Talbot GH, Bradley JS, et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. Clin Infect Dis 2009; 48: 1-12. [CrossRef]
4. Celebi S, Hacimustafaoglu M, Koksal N, Ozkan H, Cetinkaya M. Colistimethate sodium therapy for multidrug-resistant isolates in pediatric patients. Pediatr Int 2010; 52: 410-4. [CrossRef]
5. Ramasubban S, Majumdar A, Das PS. Safety and efficacy of polymyxin B in multidrug resistant Gram-negative severe sepsis and septic shock. Indian J Crit Care Med 2008; 12: 153-7. [CrossRef]
6. Falagas ME, Vouloumanou EK, Rafailidis PI. Systemic colistin use in children without cystic fibrosis: a systematic review of the literature. Int J Antimicrob Agents 2009; 33: 503. [CrossRef]
7. Cheng CY, Sheng WH, Wang JT, Chen YC, Chang SC. Safety and efficacy of intravenous colistin (colistin methanesulphonate) for severe multidrug-resistant Gram-negative bacterial infections. Int J Antimicrob Agents 2010; 35: 297-300. [CrossRef]
8. Durakovic N, Radojcic V, Boban A, Mrsic M, Sertic D, Serventi-Seiwerth R, Nemet D, Labar B. Efficacy and safety of colistin in the treatment of infections caused by multidrug-resistant Pseudomonas aeruginosa in patients with hematologic malignancy: a matched pair analysis. Intern Med 2011, 50: 1009-13. [CrossRef]
9. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections 1988. Z Arztl Fortbild (Jena) 1991; 85: 818-27.
10. Wayne PA. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; twenty-first informational supplement. Document 2011; M100-S21.
11. Falagas ME, Kasiakou SK. Colistin: the revival of polymyxins for the management of multidrug-resistant gram-negative bacterial infections. Clin Infect Dis 2005, 40: 1333-41. [CrossRef]
12. Karbuz A, Ozdemir H, Yaman A, et al. The use of colistin in critically ill children in a pediatric intensive care unit. Pediatr Infect Dis J 2014; 33: 19-24. [CrossRef]
13. Iosifidis E, Antachopoulos C, Ioannidou M, et al. Colistin administration to pediatric and neonatal patients. Eur J Pediatr 2010; 169: 867-74. [CrossRef]
14. Falagas ME, Rafailidis PI, Kasiakou SK, Hatzopoulou P, Michalopoulos A. Effectiveness and nephrotoxicity of colistin monotherapy vs. colistin-meropenem combination therapy for multidrug-resistant Gram-negative bacterial infections. Clin Microbiol Infect 2006; 12: 1227-30. [CrossRef]

15. Linden PK, Kusne S, Coley K, Fontes P, Kramer DJ, Paterson D. Use of parenteral colistin for the treatment of serious infection due to antimicrobial-resistant Pseudomonas aeruginosa. Clin Infect Dis 2003; 37: 154-60. [CrossRef]
16. Petrosillo N, Ioannidou E, Falagas ME. Colistin monotherapy vs. combination therapy: evidence from microbiological, animal and clinical studies. Clin Microbiol Infect 2008; 14: 816-27. [CrossRef]
17. Li J, Nation RL, Turnidge JD, et al. Colistin: the re-emerging antibiotic for multidrug-resistant Gram-negative bacterial infections. Lancet Infect Dis 2006; 6: 589-601. [CrossRef]
18. Landman D, Georgescu C, Martin DA, Quale J. Polymyxins revisited. Clin Microbiol Rev 2008; 21: 449-65. [CrossRef]
19. Jimenez-Mejias ME, Pichardo-Guerrero C, Marquez-Rivas FJ, Martin-Lozano D, Prados T, Pachon J. Cerebrospinal fluid penetration and pharmacokinetic/pharmacodynamic parameters of intravenously administered colistin in a case of multidrug-resistant Acinetobacter baumannii meningitis. Eur J Clin Microbiol Infect Dis 2002; 21: 212-4. [CrossRef]
20. Tamma PD, Lee CK. Use of colistin in children. Pediatr Infect Dis J 2009; 28: 534-5. [CrossRef]
21. Rosanova M, Epelbaum C, Noman A, et al. Use of colistin in a pediatric burn unit in Argentina. J Burn Care Res 2009; 30: 612-5. [CrossRef]
22. Falagas ME, Fragoulis KN, Kasiakou SK, Sermaidis GJ, Michalopoulos A. Nephrotoxicity of intravenous colistin: a prospective evaluation. Int J Antimicrob Agents 2005; 26: 504-7. [CrossRef]
23. Reed MD, Stern RC, O'Riordan MA, Blumer JL. The pharmacokinetics of colistin in patients with cystic fibrosis. J Clin Pharmacol 2001; 41: 645-54. [CrossRef]
24. Tamma PD, Newland JG, Pannaraj PS, et al. The use of intravenous colistin among children in the United States: results from a multicenter, case series. Pediatr Infect Dis J 2013; 32: 17-22. [CrossRef]
25. Karli A, Paksu MS, Karadag A, et al. Colistin use in pediatric intensive care unit for severe nosocomial infections: experience of an university hospital. Ann Clin Microbiol Antimicrob 2013; 12: 32. [CrossRef]
26. Gupta S, Govil D, Kakar PN, et al. Colistin and polymyxin B: a re-emergence. Indian J Crit Care Med 2009; 13: 49-53. [CrossRef]