Peertechz

Clinical Group

Global Journal of Infectious Diseases and Clinical Research

DOI: http://dx.doi.org/10.17352/gjidcr

ISSN: 2455-5363 CC By

J Nievas[1,2*], D Torres[3], F Nicola[1], P Bonvehí[3], L Scocozza[1], W Alcalá[3], F Herrera[3], S Relloso[1] and J Smayevsky[1]

[1]Laboratorio de Bacteriología, Micología y Parasitología, CEMIC, Buenos Aires, Argentina
[2]Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina
[3]Sección de infectología y servicio de control de infecciones

Received: 24 November, 2018
Accepted: 10 December, 2018
Published: 11 December, 2018

***Corresponding authors:** Jimena Nievas, Laboratorio de Bacteriología, Micología y Parasitología, CEMIC, Buenos Aires, Argentina, E-mail: jimenievas@hotmail.com

https://www.peertechz.com

Check for updates

Letter to Editor

Emergent of Colistin Resistant Enterobacteriaceae carrying the mcr-1 gene among clinical isolates from patients in an Argentine hospital: Clinical and microbiological aspects

The recent emergence of multidrug-resistant (MDR) or extremely drug-resistant (XDR) Gram-negative bacteria has renewed interest in colistin (Polymyxins, a family of cationic polypeptide antibiotics) as a last-resort in the treatment of severe bacterial infections [1,2], despite being a drug with potential serious adverse events (mainly high risk of nephrotoxicity) [3,4]. Acquired resistance to polymyxins is generally associated with chromosomal mutations [5,6]. However, increasing use of this antibiotic in clinical and veterinary practice has led to the emergence of mobile colistin resistance genes, including mcr-1, which was first reported in Escherichia coli in 2015 in China [7], and mcr-2, identified in Escherichia coli in 2016 in Belgium [8]. Recently, three further plasmid mediated colistin resistance genes, mcr-3, mcr-4 and mcr-5, were identified, with *Enterobacteriaceae* being the predominant hosts (particularly *Escherichia coli* and *Salmonella* spp). Mcr-1 and mcr-2 are the most frequent variants found in human clinical isolates. [7-11].

In this report, we describe the detection of mcr-1 gene in clinical isolates of colistin-resistant *Enterobacteriaceae* from a University Hospital from Buenos Aires, Argentina. Clinical and microbiological findings were also collected.

Forty clinical isolates of colistin-resistant *Enterobacteriaceae* were evaluated from August 2014 to November 2016. Twenty-two *Escherichia coli* and 18 *Klebsiella pneumoniae* were isolated from urine (25), blood culture (3), soft tissue (1), abdominal fluid (3) and rectal swabs [8]. MALDI-TOF (BD-BrukerDaltonics) was used for identification. Minimal inhibitory concentrations (MICs) were determined by Phoenix method (Becton, Dickinson) and epsilometer method according to the guidelines of the CLSI and EUCAST joint subcommittee [12]. Results were interpreted using EUCAST breakpoint as updated in 2018 (www.eucast.org). All isolates were screened by PCR for the presence of mcr-1 and mcr-2 genes as previously described [7,8]. Multilocus Sequence Type (MLST) was carried out as described previously [13] and PCR amplicons were purified with QIAquik PCR Purification Kit (QIAGEN) and were sequenced by the Sanger method Unit of Genomics Institute of Biotechnology CICVyA CNIA INTA.

The mcr-1 gene was detected in 16 isolates, 14 *Escherichia* coli and 2 *Klebsiella pneumoniae* strains, all with MICs at colistin greater than 4 µg/ml. One patient had polymicrobial infection. *Escherichia coli* isolates did not show significant antibiotic resistance; only 2 were ESBL (extended-spectrum β-lactamase) producers. One isolate of *Klebsiella pneumoniae* was multidrug-resistant (KPC positive), being sensitive only to amikacin. Of the isolates that were not positive for the mcr-1 gene (n = 24), 16 were *Klebsiella pneumoniae* (13 KPC +) and 8 *Escherichia coli* (4 ESBL +) recovered from urine (13), rectal swabs (8), blood cultures (2), and abdominal fluid (1). The mcr-2 gene was not found in any isolate. In this study the resistance mechanism to colistin of those mcr-1 and mcr-2 gene non-carrier strains were not evaluated.

Sixteen strains from 15 patients (13 adults and 2 pediatrics) were detected. The median age was 61 years (p25-75: 46.5-69). No clinical data were obtained from four patients.

All had multiple comorbidities (chronic renal failure, heart disease, renal transplantation, peripheral vascular disease, neoplasia or diabetes mellitus). The site of acquisition was

Citation: Nievas J, Torres D, Nicola F, Bonvehí P, Scocozza L, et al. (2018) Emergent of Colistin Resistant Enterobacteriaceae carrying the mcr-1 gene among clinical isolates from patients in an Argentine hospital: Clinical and microbiological aspects. Glob J Infect Dis Clin Res 4(1): 010-012.
DOI: http://doi.org/10.17352/2455-5363.000019

nosocomial in six patients, and five patients had health care-associated infections (three with recent hospitalization, one had outpatient surgery and the other had frequent contact with the health system). Nine patients had previously received antibiotics, only three were treated with colistin. The clinical source was urinary (13 patients), cutaneous (one) and abdominal (one). Ten received appropriate antibiotic treatment according to microbiological findings.

The mcr-1-positive isolates belonged to several different sequence types (STs) (Table 1), some of which have not been previously associated with mcr-1.

Plasmid-mediated colistin resistance is now emerging. In our hospital during two years (2014-2016), we detected the presence of the mcr-1 gene mainly in *Escherichia coli* and *Klebsiella pneumoniae* strains. All isolates were genetically unrelated. The occurrence of mcr-1 in clinical isolates of *Enterobacteriaceae* is alarming. The detection of these strains is of great importance, since it allows implementing corresponding actions. In hospitals, we recommended the application of contact precautions to avoid their dissemination to other patients and their transfer to other species. Moreover, we need antimicrobial stewardship programs to use these drugs responsibly, only when other options are not available. Beside this, global industrial and veterinary use of colistin should be limited to reduce the appearance of this resistance mechanism and to prevent the potential transmission from farm to humans.

Acknowledgments

This study was supported by René Baron Fundation

Table 1:

Patient	Age	Isolation date	Isolation site	Site of adquisition	Underlying conditions	Recent hospitalization	Intensive care unit admission	Previous therapy with colistin	Isolation	MIC Col ph	MIC col epsilometer	ESBL	ST
1	60	January 2016	Soft tissue	Health care associated	Diabetes mellitus, peripheral vascular diseases	No	No	No	*E. coli*	4	4	POS	69
2	67	February 2016	Urine	Hospital acquired	Kidney transplantation	Yes	Yes	Yes	*E. coli*	4	3	NEG	406
3	81	February 2016	Urine	Hospital acquired	Chronic heart failure, valvular heart failure	Yes	Yes	Yes	*E. coli*	4	4	NEG	131
4	88	March 2016	Urine	Health care associated	Valvular heart disease, Breast cancer	Yes	Yes	No	*E. coli*	4	4	NEG	5921
5	69	March 2016	Urine	Health care associated	Coronary artery disease, Stroke	Yes	Yes	Yes	*E. coli*	4	4	NEG	1485
6	87	March 2016	Urine	Hospital acquired	Coronary artery disease, valvular heart disease, chronic renal failure	Yes	Yes	No	*E. coli*	4	8	NEG	1431
7	59	March 2016	Abdomen	Hospital acquired	Chronic renal failure	Yes	Yes	No	*E. coli*	8	4	NEG	216
7	59	March 2016	Abdomen	Hospital acquired	Chronic renal failure	Yes	Yes	No	*K.pneumoniae*	8	4	NEG	11
8	36	July 2016	Urine	Health care associated	Chronic renal failure, Kidney transplantation	Yes	No	No	*E. coli*	8	16	NEG	6456
9	39	July 2016	Urine	Not Available	Not Available	Not Available	Not Available	Not Available	*E. coli*	4	4	NEG	349
10	61	July 2016	Urine	Not Available	Not Available	Not Available	Not Available	Not Available	*E. coli*	4	3	POS	1148
11	86	August 2016	Urine	Hospital acquired	Chronic renal failure, Peripheral vascular disease	Yes	No	No	*E. coli*	4	4	NEG	117
12	8	August 2016	Urine	Not Available	Not Available	Not Available	Not Available	Not Available	*K.pneumoniae*	4	2	POS	344
13	12	August 2016	Urine	Not Available	Not Available	Not Available	Not Available	Not Available	*E. coli*	4	4	NEG	227
14	54	September 2016	Urine	Hospital acquired	Chronic renal failure, Kidney transplantation	Yes	Yes	No	*E. coli*	4	4	NEG	3223
15	61	September 2016	Urine	Health care associated	Chronic renal failure	No	No	No	*E. coli*	4	4	NEG	7405

PH:Phoenix; ST:Sequence type; POS: Positive; NEG: Negative; MIC: Minimal inhibitory concentration; ESBL: Extended-spectrum β-lactamase; COL: COLISTIN

Citation: Nievas J, Torres D, Nicola F, Bonvehí P, Scocozza L, et al. (2018) Emergent of Colistin Resistant Enterobacteriaceae carrying the mcr-1 gene among clinical isolates from patients in an Argentine hospital: Clinical and microbiological aspects. Glob J Infect Dis Clin Res 4(1): 010-012.
DOI: http://doi.org/10.17352/2455-5363.000019

References

1. Falagas ME, Kasiakou SK (2005) Colistin: the revival of polymyxins for the management of multidrug-resistant Gram-negative bacterial infections. Clin Infect Dis 40: 1333–1341. Link: https://goo.gl/b7cVvU

2. Li J, Nation L, Turnidge FRAC, Milne WR, Coulthard K, et al. (2006) Colistin: the re-emerging antibiotic for multidrug-resistant Gram-negative bacterial infections. Lancet Infect. Dis 6: 589–601. Link: https://goo.gl/wCs764

3. Dixon RA, Chopra I (1986) Polymyxin Band polymyxin B nonapeptide alter cytoplasmic membrane permeability in Escherichia coli. J. Antimicrob. Chemother 18: 557–563. Link: https://goo.gl/G9WZcz

4. Brown JM (1970) Acute renal failure due to over dosage of colistin. Med. J.Aust 2: 923–924. Link: https://goo.gl/oquEXg

5. Olaitan AO, Morand S, Rolain JM (2014) Mechanisms of polymyxin resistance: acquired and intrinsic resistance in bacteria. Front Microbiol 5: 643. Link: https://goo.gl/wgXnkB

6. Falagas ME, Rafailidis PI, Matthaiou DK (2010) Resistance to polymyxins: mechanisms, frequency and treatment options. Drug Resist Updat 13: 132–138. Link: https://goo.gl/Q5mfXb

7. Liu YY, Wang Y, Walsh TR, Yi LX, Zhang R, et al. (2016) Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. Lancet Infect Dis 16: 161–168. Link: https://goo.gl/zmmUjk

8. Xavier BB, Lammens C, Ruhal R (2016) Identification of a novel plasmid mediated colistin-resistance gene, mcr-2, in Escherichia coli, Belgium, June 2016. Euro Surveill 21: 30280. Link: https://goo.gl/zDnd3v

9. Carattoli A, Villa L, Feudi C, Curcio L, Orsini S, et al. (2017) Novel plasmid-mediated colistin resistance mcr-4 gene in Salmonella and Escherichia coli, Italy 2013, Spain and Belgium, 2015 to 2016. Euro Surveill. 22: 30589. Link: https://goo.gl/M3wUTC

10. Sun J, Zhang H, Liu YH, Feng Y (2018) Towards understanding MCR-like colistin resistance. Trends in Microbiology Link: https://goo.gl/dCcDWj

11. Shizhen Ma, Sun C, Hulth A (2018) Mobile colistin resistance gene mcr-5 in porcine Aeromonas hydrophila, J Antimicrob Chemother 73: 1777–1780. Link: https://goo.gl/Zrtbh7

12. Clinical and Laboratory Standard Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) joint subcommittee. Recommendations for MIC determination of colistin (polymyxin E) as recommended by the joint CLSI-EUCAST Polymyxin Breakpoints Working Group. Link: https://goo.gl/v1qLXE

13. Wirth T, Falush D, Lan R, Colles F, Mensa P, et al. (2006) Wieler LH, Karch, H., Reeves, P. R., Maiden, M. C., Ochman, H., and Achtman M. 2006. Sex and virulence in Escherichia coli: an evolutionary perspective. Mol.Microbiol 60: 1136-1151. Link: https://goo.gl/QqpCho

Citation: Nievas J, Torres D, Nicola F, Bonvehí P, Scocozza L, et al. (2018) Emergent of Colistin Resistant Enterobacteriaceae carrying the mcr-1 gene among clinical isolates from patients in an Argentine hospital: Clinical and microbiological aspects. Glob J Infect Dis Clin Res 4(1): 010-012.
DOI: http://doi.org/10.17352/2455-5363.000019