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Journal of the Chinese Medical Association 80 (2017) 189−190

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Editorial

What can we learn from the dissemination of carbapenem-resistant *Acinetobacter baumannii* in patients with burn injury?

In this issue of the *Journal of the Chinese Medical Association*, Shoja et al[1] characterize the antimicrobial susceptibility pattern, resistance mechanisms, and typing of carbapenem-resistant *Acinetobacter baumannii* (CRAB) isolates obtained from burn patients from a single center in Iran. They found that the rate of CRAB was high (92.5%) among burn patients. The most effective drugs with *in vitro* activity against *A. baumannii* isolates in this study were colistin, polymyxin B, and ampicillin−sulbactam. Carbapenem resistance involved $bla_{\text{OXA-23-like}}$ and $bla_{\text{OXA-24-like}}$ genes. The clonal spreading of *A. baumannii* strains were identified among these burn patients. This study suggests the necessity of effective control measures against these multidrug-resistant pathogens.

A. baumannii is an important pathogen causing various nosocomial infections,[2] and has become one of the most commonly isolated pathogens in burn patients.[3] Outbreaks and rapid dissemination of CRAB strains despite prevention and control measures have been reported worldwide, which most commonly occur in intensive care units.[4−6] The spreading of multidrug-resistant *A. baumannii* (MDRAB), especially CRAB, has become a threat to public health.[2] The most important mechanism of carbapenem resistance in *A. baumannii* is the production of carbapenem-hydrolyzing β-lactamases, especially Ambler classes D-carbapenemase (OXA β-lactamases). Most of the groups of OXA-type β-lactamases have been identified on plasmids, and have a high capacity to spread.[7] The insertion sequence IS*Aba1* has been found upstream of $bla_{\text{OXA-23-like}}$ and $bla_{\text{OXA-51-like}}$ genes in *A. baumannii* and leads to overexpression of bla_{OXA} genes.[8] Other less-studied mechanisms in carbapenem resistance in *A. baumannii* are reduced outer membrane permeability, penicillin-binding protein alterations, and overexpression of the efflux pump.[9] $Bla_{\text{OXA-23-like}}$ and $bla_{\text{OXA-24-like}}$ genes were found among the *A. baumannii* isolates. Although several mechanisms would work in concert to produce the resistance phenotype, a more detailed investigation of mechanisms for carbapenem resistance is recommended for future study.

Molecular typing of the relevant *A. baumannii* isolates was a common approach for hospital outbreak investigations. The current study showed that Clones B and C were predominantly determined by repetitive sequence-based polymerase chain reaction, suggesting that these clones were possibly interward spread resulting in the infection of burn patients. Pulsed-field gel electrophoresis or multilocus variable number of tandem repeats analysis were other common methods for bacterial strain typing.[10] Multilocus sequence typing is also an effective method for comparing epidemiological investigations across different geographical areas, and the Clonal Complexes 92 were prevalent among the CRAB from burn units in several countries.[11,12] Shoja et al[1] did not provide sequencing type information in the current study. It is better to monitor the clonal complexes of CRAB strains in the burn units, given that the strains with new clonal complexes would result in future outbreaks. It is crucial to establish the strategy of better control of nosocomial CRAB infections and surveillance of this strain using molecular typing in the burn unit.

Kanamori et al[13] recently conducted a molecular investigation of three sequential outbreaks caused by MDRAB at a large academic burn center in the United States using next-generation sequencing. Next-generation sequencing is a promising molecular epidemiology method in investigations of outbreak analysis. A comparative analysis of single-nucleotide variants in bacterial genomes helps us determine the relatedness among epidemiologically linked strains, build a transmission network, and track bacterial strains of interest.[13] They found that the distribution of resistance genes varied among the three outbreaks, and demonstrated the superior resolution of outbreak transmission networks for MDRAB determined by next-generation sequencing.[13] Additional studies using whole genome sequencing of *A. baumannii* can help us design and implement more efficient interventions to control the dissemination of MDRAB in burn units.

Polymycin B and colistin have good *in vitro* activity against the CRAB in this study, which is consistent with the literature.[3,4,6,11,12] However, colistin-resistant CRAB has recently emerged as an new challenge for treatment and infection control.[5] Targeted surveillance and molecular epidemiology for this superbug plus rational use of colistin is suggested to manage this problem.[14] However, the association between antibiotics exposure and the acquisition of MDRAB or CRAB has rarely been described in the burn unit. A dust explosion

http://dx.doi.org/10.1016/j.jcma.2016.12.004

occurred on June 27, 2015 in Taiwan and more than 400 healthy young people were injured by the accident. Shie et al[15] conducted a study at Chang Gung Memorial Hospital, a medical center in Northern Taiwan, to investigate the association of carbapenem exposure with the occurrence of MDRAB in burn patients from this dust explosion. MDRAB isolates detected from any sites during the 1st month of admission were identified in nine of 42 patients (21%). Both the acquisition and disappearance of MDRAB were closely related to carbapenem exposure in these critically ill patients. This investigation indicated that early-discontinued use of carbapenem could be an essential practice for control of MDRAB. The findings from a homogeneous group of critically ill patients with burn injuries provide insight about the role and importance of antimicrobial stewardship to control MDRAB in burn units, which is less frequently addressed in the literature. MDRAB or CRAB was also the predominant pathogen isolated from burn patients in other medical centers in Northern Taiwan (data not shown). More informative data regarding infection control or treatment for this multidrug resistant pathogen from other burn units in Taiwan would be expected in the future.

Conflicts of interest

The author declares that he has no conflicts of interest related to the subject matter or materials discussed in this article.

References

1. Shoja S, Moosavian M, Rostami S, Farahani A, Peymani A, Ahmadi K, et al. Dissemination of carbapenem resistant *Acinetobacter baumannii* in patients with burn injuries. *J Chin Med Assoc* 2017;**80**:245−52.
2. Potron A, Poirel L, Nordmann P. Emerging broad-spectrum resistance in *Pseudomonas aeruginosa* and *Acinetobacter baumannii*: mechanisms and epidemiology. *Int J Antimicrob Agents* 2015;**45**:568−85.
3. Bahemia IA, Muganza A, Moore R, Sahid F, Menezes CN. Microbiology and antibiotic resistance in severe burns patients: a 5 year review in an adult burns unit. *Burns* 2015;**41**:1536−42.
4. Ye D, Shan J, Huang Y, Li J, Li C, Liu X, et al. A gloves-associated outbreak of imipenem-resistant *Acinetobacter baumannii* in an intensive care unit in Guangdong, China. *BMC Infect Dis* 2015;**15**:179.
5. Oikonomou O, Sarrou S, Papagiannitsis CC, Georgiadou S, Mantzarlis K, Zakynthinos E, et al. Rapid dissemination of colistin and carbapenem resistant *Acinetobacter baumannii* in central Greece: mechanisms of resistance, molecular identification and epidemiological data. *BMC Infect Dis* 2015;**15**:559.
6. Mathlouthi N, El Salabi AA, Ben Jomàa-Jemili M, Bakour S, Al-Bayssari C, Zorgani AA, et al. Early detection of metallo-β-lactamase NDM-1- and OXA-23 carbapenemase-producing *Acinetobacter baumannii* in Libyan hospitals. *Int J Antimicrob Agents* 2016;**48**:46−50.
7. Evans BA, Amyes SG. OXA β-lactamases. *Clin Microbiol Rev* 2014;**27**:241−63.
8. Turton JF, Woodford N, Glover J, Yarde S, Kaufmann ME, Pitt TL. Identification of *Acinetobacter baumannii* by detection of the bla_{OXA-51}-like carbapenemase gene intrinsic to this species. *J Clin Microbiol* 2006;**44**:2974−6.
9. Bonnin RA, Nordmann P, Poirel L. Screening and deciphering antibiotic resistance in *Acinetobacter baumannii*: a state of the art. *Expert Rev Anti Infect Ther* 2013;**11**:571−83.
10. Azimi L, Talebi M, Khodaei F, Najafi M, Lari AR. Comparison of multiple-locus variable-number tandem-repeat analysis with pulsed-field gel electrophoresis typing of carbapenemases producing *Acinetobacter baumannii* isolated from burn patients. *Burns* 2016;**42**:441−5.
11. Farshadzadeh Z, Hashemi FB, Rahimi S, Pourakbari B, Esmaeili D, Haghighi MA, et al. Wide distribution of carbapenem resistant *Acinetobacter baumannii* in burns patients in Iran. *Front Microbiol* 2015;**6**:1146.
12. Huang G, Yin S, Gong Y, Zhao X, Zou L, Jiang B, et al. Multilocus sequence typing analysis of carbapenem-resistant *Acinetobacter baumannii* in a Chinese burns institute. *Front Microbiol* 2016;**7**:1717.
13. Kanamori H, Parobek CM, Weber DJ, van Duin D, Rutala WA, Cairns BA, et al. Next-generation sequencing and comparative analysis of sequential outbreaks caused by multidrug-resistant *Acinetobacter baumannii* at a large academic burn center. *Antimicrob Agents Chemother* 2015;**60**:1249−57.
14. Giamarellou H. Epidemiology of infections caused by polymyxin-resistant pathogens. *Int J Antimicrob Agents* 2016;**48**:614−21.
15. Shie SS, Huang PY, Ye JJ, Wu YM, Wu TS, Wu TL, et al. *Emergence and vanishment of multidrug-resistant Acinetobacter baumannii on healthy youngsters concurrently burned in a dust explosion in Taiwan: the implication for antimicrobial stewardship*. ASM Microbe; 2016. Oral Abstract Presentations, Session 332, http://files.abstractsonline.com/SUPT/1/4060/AllOralAbstracts.pdf [Accessed 1 Feb 2017].

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