Extensive colonization with carbapenemase-producing microorganisms in Romanian burn patients: infectious consequences from the Colectiv fire disaster

L. E. Pirii1 · A. W. Friedrich1 · J. W.A. Rossen1 · W. Vogels2,3 · G. I. J. M. Beerthuizen4 · M. K. Nieuwenhuis5 · A. M. D. Kooistra-Smid1,2 · E. Bathoorn1

Received: 29 August 2017 / Accepted: 9 October 2017 / Published online: 23 October 2017
© The Author(s) 2017. This article is an open access publication

Abstract Health care of severe burn patients is highly specialized and may require international patient transfer. Burn patients have an increased risk of developing infections. Patients that have been hospitalized in countries where carbapenemase-producing microorganisms (CPMO) are endemic may develop infections that are difficult to treat. In addition, there is a risk on outbreaks with CPMOs in burn centers. This study underlines that burn patients may extensively be colonized with CPMOs, and it provides best practice recommendations regarding clinical microbiology and infection control. We evaluated CPMO-carriage and wound colonization in a burn patient initially treated in Romania, and transported to the Netherlands. The sequence types and acquired beta-lactamase genes of highly-resistant microorganisms were derived from next generation sequencing data. Next, we searched literature for reports on CPMOs in burn patients. Five different carbapenemase-producing isolates were cultured: two unrelated OXA-48-producing Klebsiella pneumoniae isolates, OXA-23-producing Acinetobacter baumanii, OXA-48-producing Enterobacter cloacae, and NDM-1-producing Providencia stuartii. Also, multi-drug resistant Pseudomonas aeruginosa isolates were detected. Among the sampling sites, there was high variety in CPMOs. We found 46 reports on CPMOs in burn patients. We listed the epidemiology of CPMOs by country of initial treatment, and summarized recommendations for care of these patients based on these reports and our study.

Keywords Carbapenemase · CPE · Burn patients · Infection control · Review · Molecular epidemiology

Introduction

In October 2015, the crowded nightclub Colectiv in Bucharest, Romania caught on fire due to indoor use of pyrotechnics. In total, 64 visitors died from burn wounds and/or inhalation of smoke, and 144 were injured. The injured visitors were immediately transported to 12 nearby hospitals in Bucharest and Ilfov County for medical care [1]. Since appropriate medical care could not be provided for all patients, international aid was requested. About 80 patients were transported to various countries, including 16 to The Netherlands and Belgium, after they had been hospitalized for over a week in Romania.

Romania is a country with a high prevalence of carbapenemase-producing microorganisms (CPMO) [2, 3]. As burn patients have a high risk of developing infectious complications, this is a serious problem to be reckoned with. Wound infection with CPMO complicates the treatment of patients with burns [4, 5]. Patients suffering from these kinds of infections have to be treated with last-line antibiotic schemes. These schemes are most often sub-optimal for treatment of the infection and have more adverse effects. In addition to the impact of CPMO-infection on the treatment of the...
individual patient, the introduction of CPMOs in the hospital also may lead to nosocomial transmission of CPMO resulting in hospital outbreaks.

Burn wounds are highly prone to long-term colonization by nosocomial bacteria. It has been reported that in more than 90% of patients the wounds were colonized by the seventh day, and that constitution of colonizing microorganisms in individual burn wounds changes over time [6, 7]. Wound colonization can subsequently result in severe invasive infection, a leading cause of mortality in patients with burn injury [8].

Restrictive and targeted use of antibiotics is important in treatment of burn patients, in particular in those with CPMOs. Guidelines from the European Burns Association recommend the use of “topical creams with good antimicrobial effects without the risk for resistance or allergy”. “The use of prophylactic systemic antibiotics is not supported by evidence” [9, 10]. Infections are most often caused by the microorganisms that colonize the burn wounds [11, 12]. Thus, it is important to culture wounds on admission, also before signs of infection, to know which antibiotics to start in case of infection.

Here, we describe the diversity in CPMO cultured at admission from several burn wounds and body sites in a burn patient from the Colectiv fire disaster transported to a dedicated Burn Centre in the Netherlands. Next, we performed an analysis of literature focusing on CPMO in patients with burns. By this, we show that the presented case of extensive burn wound colonization with CPMO is not an exception. Finally, we provide specific recommendations for medical care of burn patients transported from CPMO endemic regions to other countries with low CPMO prevalence. For non-endemic countries such as the Netherlands, international transfer of patients carrying CPMOs imposes a risk on dissemination to other hospitalized patients.

Case description

A Romanian victim of the Colectiv fire disaster had been admitted to “Spitalul Clinic de Urgenta” in Bucharest on October 31st 2015 with a total body surface area (TBSA) burn of approximately 30%. The patient was in his 20s and had an uncomplicated medical history before this incident.

There were IIA–IIB degree burn lesions on the face, posterior cervical area, right scapular area, deltoid area bilaterally and IIB–III degree burns on both hands, forearms, and scalp. Meshed split skin grafting had been performed to cover the burns on his right lower arm and hand. On the IC unit, the patient had received broad-spectrum empirical antibiotic therapy with Piperacillin/ Tazobactam 4.5 g tid and Linezolid 600 mg bid. Based on results of wound cultures that revealed Acinetobacter spp., antibiotics were switched to Colistin 2 million units tid for the treatment of wound infection. For topical treatment of the wounds, silversulfadiazine, kanamycine ointments, and betadine scrub were used. No additional information on the microbiological cultures was mentioned in the Romanian discharge notes.

The patient was transported by airplane and ambulance to the Burn Centre of the Martini Hospital (BCMH) in Groningen, The Netherlands on November 7th 2015, 7 days after the incident. Upon admission to the BCMH, the patient’s TBSA burned was still approximately 10%. Admission cultures taken from the wounds and body sites (nose, throat, perineum) showed extensive colonization with CPMOs (see results section). Following regular Dutch infection control recommendations, the patient was consequently placed in isolation. However, in this phase there was no need for treatment with systemic antibiotics. The burn wounds were topically treated with silversulfadiazine ointment. After 12 days, definitive covering of non-healing sites was opportune after enlargement of autologous donor skin in a ratio of 1:1.5. Skin defects on both hands and ears were covered with skin grafts taken from the right upper leg. Good take of the grafts was observed in the weeks after surgery. Pressure gloves were used to augment the healing of the hands. Through extensive physical and occupational therapy, the patient regained his ability to perform normal daily activities. The patient was discharged from the hospital after 34 days.

After discharge, the patient’s air-locked room with sanitary facility was disinfected. Subsequently taken environmental samples were negative.

Methods

Culture and characterization of bacterial isolates

Upon admission, screening throat, nose, perineum, rectum, and wound sample cultures were taken for detection of MRSA and highly-resistant gram negative bacteria (HRGN). Cultures from wounds were taken from the following locations: the anterior left elbow, the left and right ear, right shoulder and the left groin on November 9th; the left palm, and right upper back side on November 16th; the dorsum of the left hand, the right fingers and a repeated culture of right and left ear on November 30th. In total, 29 cultures were taken during the hospital stay: 14 screening cultures, three urine cultures, and 12 wound cultures. Burn wounds were cultured using sets of RODAC plates with five different media: blood agar +5% sheepblood (BA + 5%SB), colistin oxolinic-acid blood agar, mannitol salt agar, MacConkey agar no.3 + crystalviolet, Sabouraud dextrose agar + aztreonam/vancomycin (Mediprodutcs, the Netherlands). For sampling, the plates were applied directly on the wounds. The plates were incubated for 48 h at 35 °C. Screening for meticillin-resistant Staphylococcus aureus (MRSA) was done with Xpert MRSA Gen3 assay (Cepheid, France) and by culture using
BA + 5%SB and CHROMagar ID MRSA (bioMérieux, France) plates. Species determination of isolates was performed by using Maldi-TOF MS (bioMérieux, France). Antibiotic susceptibility was tested using VITEK 2 XL (bioMérieux, France). Minimal inhibitory concentrations (MICs) to tigecyclin, amikacin, and fosfomycin were tested using Etest® according to manufacturer’s guidelines on Mueller Hinton agar (AB Biodisk, Germany). Susceptibility was interpreted according to EUCAST guidelines [13]. Using whole genome sequencing data, we characterized the CPMOs isolates and identified acquired resistance genes as described before [14]. In short, genomic DNA was extracted and prepared libraries were run on a MiSeq platform (Illumina, USA) generating paired-end 250-bp reads. De novo assembly of paired-end reads was performed using CLC Genomics Workbench v7.5 (QIAGEN, Germany) after quality trimming (Qs ≥ 20) with optimal word size. The acquired antimicrobial resistance genes were identified by uploading assembled genomes to the Resfinder server v2.1 [15]. The MLST-types were assessed using SeqSphere v3.4.0 (Ridom GmbH, Germany).

Patient informed consent and approval of local ethical committee have been obtained. All of the assessed culture samples were taken in routine diagnostics.

Literature analysis

We performed a literature search in PubMed to assess the epidemiology of CPMOs in burn wound care and recommendations for care of these patients by the following search strategy: ((burn*[MeSH] OR burn*[TIAB] OR burn*[All Fields]) AND ((carbapenemase*[MeSH] OR carbapenemase*[All Fields] OR carbapenem-resistant*[MeSH] OR carbapenem-resistant*[All Fields] OR carbapenem producing organisms*[MeSH] OR carbapenemase producing organisms*[All Fields] OR carbapenemase producing Enterobacteriaceae*[MeSH] OR carbapenemase producing Enterobacteriaceae*[All Fields] OR panresistant*[MeSH] OR panresistant*[All Fields] OR carbapenemase producing microorganisms*[MeSH] OR carbapenemase producing microorganisms*[All Fields])). Studies up to December 2016 were retrieved and screened by their title and abstract for their relevancy on the topic.

Results

Cultures

MRSA diagnostics were all negative; methicillin-susceptible S. aureus was cultured from nose and the burn wounds. We present an overview of characteristics of the isolated HRGNs in Table 1. In total, six different HRGNs were detected: five different carbapenemase-producing isolates, and one carbapenem-resistant Pseudomonas aeruginosa isolate. The carbapenemase-producing isolates included OXA-48-producing Klebsiella pneumoniae isolates of ST type 147, and 395, OXA-23-producing Acinetobacter baumanii ST type 231, OXA-48-producing Enterobacter cloacae ST type 114, and NDM-1-producing Providencia stuartii.

An overview of all body locations and isolated HRGNs is presented in Fig. 1. Screening cultures for carriage of HRGNs were positive in nose (4 different isolates), perineum (3 different isolates), rectum (1 isolate) and throat (1 isolate). Cultures from the wound sites showed varying colonization with HRGNs. All sampled wound sites were colonized by HRGNs. The highest number of HRGNs 5/6 were isolated from the groin wound, a donor site wound after the grafting procedures done in Romania. The MDR Pseudomonas aeruginosa isolates were exclusively detected in samples from the upper body. We observed differences in colonization in similar body regions: the right forearms was positive for single isolates of highly-resistant Enterobacter cloacae, Pseudomonas aeruginosa, and Acinetobacter baumanii, whereas the left forearm sample grew Klebsiella pneumoniae. The matching culture results between urine and both hands are remarkable: in all three samples the NDM-1-producing Providencia stuartii were cultured.

All isolates tested resistant to cotrimoxazol, ciprofloxacin and aminoglycosides, except for Klebsiella pneumoniae isolates of ST 395 and OXA-48-producing Enterobacter cloacae which were susceptible to amikacin. Only the NDM-1 producing Providencia stuartii NDM-1 and Klebsiella pneumoniae ST type 147 were susceptible to fosfomycin. Two colistin-resistant isolates were detected: an OXA-48-producing Providencia stuartii, which is intrinsically resistant, and an NDM-1-producing Klebsiella pneumoniae.

In addition, multiple carbapenem-non-susceptible Pseudomonas aeruginosa isolates of MLST ST235 were grown. The Pseudomonas isolates were multidrug resistant, testing resistant to antipseudomonal beta-lactams, fluoroquinolones, and aminoglycosides, and susceptible to colistin.

Review

In our review search we found 84 reports on CPMOs in burn wound care. Of these, 38 were off-topic, thus we included 46 reports. To assess the epidemiology, we present a country by country overview (Table 2) of reports on CPMOs in burn care centers. The country of initial care is shown.

CPMOs in burn patients have been reported from institutions over all continents.

The CPMOs included Acinetobacter baumanii, Pseudomonas aeruginosa, and the following Enterobacteriaceae: Escherichia coli, Klebsiella oxytoca and...
Table 1  Characteristics of the isolated highly-resistant Gram negative bacteria (HRGNs)

| Isolate       | Date       | Sample     | MIC (mg/L) | MIC IMP (mg/L) | Sensitivity | MIC COL (mg/L) | MIC TIG (mg/L) | Bla-genesa | ST type |
|---------------|------------|------------|------------|----------------|-------------|----------------|----------------|-------------|---------|
| A. baumanii   | 30-11-2015 | Left ear   | ≥16 R      | ≥16 R         | R R R R      | R R            | R              | <0.5 S     | 3 R     | OXA-23; OXA-64 | ST 231 |
| E. cloacae    | 7-11-2015  | Perineum   | ≥16 R      | ≥16 R         | R R R R      | R R            | R              | <0.5 S     | 2 R     | OXA-48; CTX-M 15; OXA-1; TEM-1b; ACT-16 | ST 114 |
| K. pneumoniae | 9-11-2015  | Right ear  | ≥16 R      | ≥16 R         | R R R S      | R R            | R              | =16 R      | 3 S     | OXA-48; CTX-M 15; OXA-1; NDM-1; TEM-1b | ST 147 |
| K. pneumoniae | 7-11-2015  | Perineum   | >16 R      | >16 R         | S R R R      | R R            | R              | <0.5 S     | 1.5 S   | OXA-48; CTX-M 15; OXA-1; TEM-1b; SHV-11 | ST 395 |
| K. pneumoniae | 30-11-2015 | Perineum   | ≥16 R      | ≥16 R         | R R R R      | R R            | R              | ≥16 R      | R      | OXA-48; CTX-M 15; OXA-1; TEM-1b; SHV-11 | ST 395 |
| K. pneumoniae | 7-11-2015  | Rectum     | >32 R      | 12 R          | S R R R      | R R            | R              | <0.5 S     | 2 R     | OXA-48; CTX-M 15; OXA-1; TEM-1b; SHV-11 | ST 395 |
| P. stuartii   | 9-11-2015  | Left groin | >16 R      | >16 R         | R R R R      | R R            | R              | >16 R      | 3 R     | NDM-1; OXA-10; CMY-4 | n.a. |
| P. stuartii   | 23-11-2015 | Perineum   | >16 R      | >16 R         | R R R R      | R R            | R              | >16 R      | Not tested | NDM-1; OXA-10; CMY-4 | n.a. |
| P. stuartii   | 23-11-2015 | Urine      | >16 R      | >16 R         | R R R R      | R R            | R              | >16 R      | Not tested | NDM-1; OXA-10; CMY-4 | n.a. |
| P. stuartii   | 30-11-2015 | Perineum   | 2 S        | >16 R         | R R R R      | R R            | R              | >16 R      | Not tested | NDM-1; OXA-10; CMY-4 | n.a. |
| P. aeruginosa | 7-11-2015  | Throat     | 2 S        | 2 S           | R R Not tested | R R            | R              | 0.5 S      | Not tested | None detected | ST 235 |
| P. aeruginosa | 23-11-2015 | Throat     | 4 I        | 1 S           | R R Not tested | R R            | R              | <0.5 S     | Not tested | None detected | ST 235 |
| P. aeruginosa | 30-11-2015 | Left dorsum hand | 3 I | 2 S | R R Not tested | R R | R | <0.5 S | Not tested | None detected | ST 235 |

ak amikacin, gn gentamicin, sxt trimethoprim/sulfamethoxazole, cip ciprofloxacin, fos fosfomycin, tig tigecycline, col. colistine, n.a. not available

a Acquired beta-lactamase genes are presented
Klebsiella pneumoniae, Enterobacter cloacae, and Providencia stuartii. In these CPMOs, carbapenemase subtypes of KPC, NDM, VIM, IMP and OXA were detected.

The highest number of reports originated from Iran. In 17 publications, patients with burns hospitalized in Iran with carbapenem-resistant Acinetobacter baumanii and Pseudomonas aeruginosa were reported. The great diversity of carbapenemases detected in Acinetobacter baumanii in the Iranian studies is remarkable. One isolate even produced KPC, VIM and OXA-23, representing three different carbapenemases [39].

With our search, we retrieved two studies that described victims of the Colectiv fire disaster from Romania who were treated in England. As in our study, each of them was colonized and or infected with an extraordinary diversity of CPMOs. NDM-producing Klebsiella pneumoniae, OXA-48-producing Klebsiella pneumoniae and Escherichia coli, OXA-40-producing Acinetobacter baumanii and carbapenem-resistant Pseudomonas aeruginosa were isolated from these patients [13, 14]. The prolonged duration of hospitalization in Romania may have contributed to this extensive colonization with CPMOs. No transfer information had been given to their service about previous microbiology results. One of their patients died of pan-resistant NDM-producing Klebsiella pneumoniae septicemia within 48 h of admission. A second case died from severe sepsis due to extensive infected burn injuries: a pan-resistant OXA-48-producing Klebsiella pneumoniae grew in the blood culture. Our patient fortunately did not develop infections requiring treatment with systemic antibiotics. Nonetheless, we proactively tested antibiotic susceptibilities for last-line treatment options in all the isolates.

Fig. 1 Overview of all body locations and isolated HRGNs. CPE Carbapenemase producing Enterobacteriacae, CPAB Carbapenemase producing Acinetobacter baumanii, MDR Multidrugresistant

Recommendations

The Netherlands is a non-endemic country for CPMOs. To maintain this status, we put maximum effort in surveillance and infection control to prevent unnoticed introduction and dissemination of CPMOs. Experience with treatment of burn patients from endemic countries in countries with low CPMO prevalence has been described in six studies [18, 19, 26, 28, 56, 57]. In Table 3, we provide an overview of advice based on these studies completed by recommendations from the present study. All of the studies were alert for the serious risk of CPMO-carriage in transferred patients after hospitalization abroad. Outbreaks with CPMO or outbreak strains or evaluation of contact precautions after an outbreak were described in eight studies [19, 23, 26, 27, 51, 57, 62, 63]. To reduce the risk of transmission of CPMOs, patients should be treated in contact isolation in single-patient rooms until culture results are known. Not only can bacteria spread directly by hand contacts [28, 64–66], but also indirectly through the environment and by medical equipment [28, 56, 64–66]. Therefore, we recommend standardized guidelines for the transfer of severely-ill patients between European countries, where detailed procedures on communication, screening and infection prevention measures are described. Especially for specific treatment and in case of international help, clinical staff organizing treatment abroad need to be aware of such guidelines. Furthermore, we recommend education of staff in hand hygiene and isolation precautions, enhancement of disinfection of patient rooms, and single-use of medical equipment if feasible for treatment of burn patients. When transmission of CPMOs is suspected, isolates should be typed and their molecular
characteristics should be compared to confirm the clonal spread. Based on this, an outbreak investigation should be started. Control of CPMO or the roll-back of CPMO is today one of the most important goals.
Samples of throat, nose, rectum, perineum, and all wound sites should be taken at admission to detect all CPMOs and MRSAs carried by the patient. It is important to detect all CPMOs and test their susceptibility patterns, so that targeted therapy can be started in case of systemic infections. Ideally, treating clinicians should already be informed upon patient admission about culture results from the hospital of discharge. For this purpose, good communication within health care networks is needed. This is may be facilitated by the European Burns Association.

To summarize, we showed that burn patients that have been hospitalized in a CPMO endemic country can be colonized by an extensive variety of CPMOs. CPMO presence may differ among body locations, thus we recommend culturing of multiple wound sites. Burn wound colonization by CPMOs is a worldwide problem. There is a high risk for burn patients to develop invasive infections by CPMOs, which require targeted antibiotic therapy. In addition, there is the risk on hospital outbreaks by these CPMOs. Therefore, medical care facilities treating patients with burns transported from endemic regions should have advanced medical microbiology, and infection control systems in place to detect CPMOs, treat infections, and prevent onward transmission.

Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

References

1. Cojocariu M, Constanda A (2015) Incendiu in Clubul Colectiv din Bucuresti: 27 de morti, 146 de persoane internate. Marturiiile supravietuitorilor si repartizarea ranitilor. Adevarol.ro
2. Grundmann H, Glasner C, Albiger B, Aanensen DM, Tomlinson CT, Andrasevic AT, Canton R, Carmeli Y, Friedrich AW, Giske CG, Glupczynski Y, Gniadkowski M, Livermore DM, Nordmann P, Poirel L, Rossolini GM, Seifert H, Vatopoulos A, Walsh T, Woodford N, Monnet DL, European Survey of Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) Working Group (2017) Occurrence of carbapenemase-producing Klebsiella pneumoniae and Escherichia coli in the European survey of carbapenemase-producing Enterobacteriaceae (EuSCAPE): A prospective, multinational study. Lancet Infect Dis 17:153–163
3. Lixandru BE, Cotar AI, Strait M, Usein CR, Cristea D, Ciontea S, Tatu-Chitoiu D, Codita I, Rafila A, Nica M, Buzea M, Baicus A, Ghita MC, Nistor I, Tuchilus C, Indreas M, Antohe F, Glupczynski Y, Grundmann H, Jasir A, Damian M (2015) Carbapenemase-producing Klebsiella pneumoniae in Romania: a six-month survey. PLoS One 10:e0143214
4. Wisplinghoff H, Perbix W, Seifert H (1999) Risk factors for nosocomial bloodstream infections due to Acinetobacter baumannii: A case-control study of adult burn patients. Clin Infect Dis 28:59–66
5. Alaghehbandan R, Azimi L, Rastegar Lari A (2012) Nosocomial infections among burn patients in Teheran, Iran: A decade later. Ann Burns Fire Disasters 25:3–7
6. Taneja N, Chari P, Singh M, Singh G, Biswal M, Sharma M (2013) Evolution of bacterial flora in burn wounds: Key role of environmental disinfection in control of infection. Int J Burns Trauma 3:102–107
7. Raz-Pasteur A, Hussein K, Finkelstein R, Ullmann Y, Egozi D (2013) Blood stream infections (BSI) in severe burn patients–early and late BSI: A 9-year study. Burns 39:636–642
8. Wang Y, Tang HT, Xia ZF, Zhu SH, Ma B, Wei W, Sun Y, Lv KY (2010) Factors affecting survival in adult patients with massive burns. Burns 36:57–64
9. Ugburo AO, Atoyebi OA, Oyeneyin JO, Sowemimo GOA (2004) An evaluation of the role of systemic antibiotic prophylaxis in the control of burn wound infection at the Lagos University teaching hospital. Burns 30:43–48
10. European Burns Association (2015) European Practice Guidelines for Burn Care. European Burns Association, The Netherlands
11. Church D, Elsayed S, Reid O, Winston B, Lindsay R (2006) Burn wound infections. Clin Microbiol Rev 19:403–434
12. Patel BM, Paratz JD, Mallet A, Lipman J, Rudd M, Muller MJ, Paterson DL, Roberts JA (2012) Characteristics of bloodstream infections in burn patients: an 11-year retrospective study. Burns 38:685–690
13. Kahlmeter G, Brown DFJ, Goldstein FW, MacGowan AP, Mouton JW, Odenholt I, Rodloff A, Soussy C, Steinbakk M, Soriano F, Stetsiouk O (2006) European committee on antimicrobial susceptibility testing (EUCAST) technical notes on antimicrobial susceptibility testing. Clin Microbiol Infect 12:501–503
14. Zhou K, Lokate M, Deurenberg RH, Tepper M, Arends JP, Raangs EG, Lo-Ten-Foe J, Grundmann H, Rossen JW, Friedrich AW (2016) Use of whole-genome sequencing to trace, control and characterize the regional expansion of extended-spectrum beta-lactamase producing ST15 Klebsiella pneumoniae. Sci Rep 6:20840
15. Zankari E, Hasman H, Cosentino S, Vestergaard M, Rasmussen S, Lund O, Aarestrup FM, Larsen MV (2012) Identification of acquired antimicrobial resistance genes. J Antimicrob Chemother 67:2760–2664
16. McGann P, Hang J, Clifford RJ, Yang Y, Kwak YI, Kuschner RA, Lesho EP, Waterman PE (2012) Complete sequence of a novel 178-kilobase plasmid carrying bla(NDM-1) in a Providencia stuartti strain isolated in Afghanistan. Antimicrob Agents Chemother 56:1673–1679
17. Meradji S, Barguigou A, Bentakou MC, Nayke Y, Zerouali K, Mazou D, Chettibi H, Timinoumi M (2016) Epidemiology and virulence of VIM-4 metallo-beta-lactamase-producing Pseudomonas Aeruginosa isolated from burn patients in eastern Algeria. Burns 42:906–918
18. Moisessnet D, Richard P, Granados M, Merens A, Fournier D, Fines-Guyon M, Arlet G, Vu-Thien H (2015) Transfer between an Algerian and a French hospital of four multi-drug resistant bacterial strains together via a single patient. Int J Burns Trauma 5:82–85
19. De Vos D, Parnay JP, Bilocq F, Jennes S, Verbeken G, Rose T, Dijkshoorn L (2016) Molecular epidemiology and clinical impact of carbapenem-hydrolyzing-beta-lactamase genes are widespread among hospitalised burn patients in Tehran. J Infect Public Health 8:533–542
20. Azimi L, Talebi M, Pourshafie MR, Owlia P, Rastegar Lari A (2015) Characterization of Carbapenemases in extensively drug resistance Acinetobacter baumannii in a burn care center in Iran. Int J Mol Cell Med 4:46–53
21. Salimizand H, Noori N, Meshkat Z, Ghazvini K, Amel SJ (2015) Prevalence of Carbapenem resistant Acinetobacter Baumannii harboring ISAba1/bla OXA-23-like family in a burn unit. Burns 41:1100–1106
22. Nasrolahei M, Zahedi B, Bahador A, Saghi K, Kholid S, Jalalvand N, Esmaeili D (2014) Detection of blaOXA-23, ISAba1, Aminoglycosides resistant genes among burned & ICU patients in Tehran and Sari, Iran. Ann Clin Microbiol Antimicrob 13:0
23. Rastegar Lari A, Alaghhehbandan R, Asghari B, Lari ER (2015) Inhibitory-based method for detection of Metallo beta-lactamase producing Pseudomonas Aeruginosa isolated from burn patients. J Pharm Pharm Sci 18:533–542
43. Farajzadeh Sheikh A, Rostami S, Jolodar A, Tabatabaiefar MA, Khovars F, Saki A, Shoja S, Sheikh R (2014) Detection of metallo-beta-lactamases among carbapenem-resistant Pseudomonas aeruginosa. Jundishapur J Microbiol 7:e12289
44. Salimi F, Eftekhar F (2014) Prevalence of blaIMP, and blaVIM gene carriage in metallo-carbapenem-lactamase-producing burn isolates of Pseudomonas aeruginosa in Tehran. Turk J Med Sci 44:511–514
45. Neyestanaki DK, Mirsalehian A, Rezagholizadeh F, Jabalameli F, Taherikalani M, Emaneini M (2014) Determination of extended spectrum beta-lactamases, metallo-beta-lactamases and AmpC-beta-lactamases among carbapenem resistant Pseudomonas Aeruginosa isolated from burn patients. Burns 40:1556–1561
46. Lari AR, Azimi L, Rahbar M, Alaghehbandan R, Sattarzadeh-Tahrizi M (2014) First report of Klebsiella pneumoniae carbapenemase-producing Pseudomonas aeruginosa isolated from burn patients in Iran; phenotypic and genotypic methods. GMS Hyg Infect Control 9:Doc096
47. Yousefi S, Nahaei M, Farajnia S, Ghojadeh M, Akhi M, Sharifi Y, Milani M, Ghotaslou R (2010) Class 1 integron and Imipenem resistance in clinical isolates of Pseudomonas aeruginosa: Prevalence and antibiotic susceptibility. Iran J Microbiol 2:115–121
48. Eftekhar F, Naseh Z (2015) Extended-spectrum beta-lactamase and carbapenemase production among burn and non-burn clinical isolates of Klebsiella Pneumoniae. Iran J Microbiol 7:144–149
49. Rastegar Lari A, Azimi L, Rahbar M, Fallah F, Alaghehbandan R (2013) Phenotypic detection of Klebsiella Pneumoniae carbapenemase among burn patients: First report from Iran. Burns 39:174–176
50. Benenson S, Navon-Venezia S, Carmeli Y, Adler A, Shrailevitz J, Moses AE, Block C (2009) Carbapenem-resistant Klebsiella Pneumoniae endocarditis in a young adult. Successful treatment with gentamicin and colistin. Int J Infect Dis 13:295
51. Casini B, Selvi C, Cristina ML, Totaro M, Costa AL, Valentin P, Barnini S, Baggiani A, Tagliaferri E, Privitera G (2017) Evaluation of a modified cleaning procedure in the prevention of carbapenem-resistant Acinetobacter Baumannii clonal spread in a burn intensive care unit using a high-sensitivity luminometer. J Hosp Infect 95:46–52
52. Mathlouthi N, El Salahi AA, Ben Jamaa-Jemili M, Bakour S, Al-Baysasi C, Zorgani AA, Kraiena A, Elahmer O, Okdah L, Rolain JM, Chouchani C (2016) Early detection of metallo-beta-lactamase NDM-1 and OXA-23 carbapenemase-producing Acinetobacter Baumannii in Libyan hospitals. Int J Antimicrob Agents 48:46
53. Baljin B, Baldan G, Chimeddorj B, Tulgaak K, Gunchin B, Sandag T, Pfeffer K, Mackenzie CR, Wendel AF (2016) Faecal carriage of gram-negative multidrug-resistant bacteria among patients hospitalized in two centres in Ulaanbaatar, Mongolia. PLoS One 11: e0168146
54. Sepehri S, Poliquin G, Alfattah N, Boyd D, Mulvey M, Denisuk A, Fanella S, Karlowsky J, Walkty A (2014) Osteomyelitis due to multiple carbapenemase-producing gram-negative bacteria: the first case report of a GES-13-producing Pseudomonas aeruginosa isolate in Canada. Can J Infect Dis Med Microbiol 25:229–231
55. Novak P, Paluchowska P, Budak A (2012) Distribution of blaOXA genes among carbapenem-resistant Acinetobacter Baumannii nosocomial strains in Poland. New Microbiol 35:317–325
56. Garvey MI, Bradley CW, Jumaa P (2016) Environmental decontamination following occupancy of a burns patient with multiple carbapenemase-producing organisms. J Hosp Infect 93:136–140
57. Maillet M, Pelloux I, Forli A, Vancoetsen K, Cheong Sing JS, Marfaing S, Ducki S, Batailler P, Mallaret MR (2014) Nosocomial transmission of carbapenem-resistant Pseudomonas Aeruginosa among burn patients. Infect Control Hosp Epidemiol 35:597–599
58. Belotti PT, Thabet L, Laffargue A, Andre C, Coulange-Mayonne M, Apin C, Messadi A, MFali F, Quentin C, Dubois V (2015) Description of an original integron encompassing blaVIM-2, qnrVC1 and genes encoding bacterial group II intron proteins in Pseudomonas Aeruginosa. J Antimicrob Chemother 70:2237–2240
59. Zoghlami A, Kanzari L, Boukaida J, Messadi AA, Ghanem A (2012) Epidemiological profile and antibiotic resistance of Pseudomonas aeruginosa isolates in burn and traumatology center in Tunisia over a three-year period. Tunis Med 90:803–806
60. Altoparlak U, Aktas F, Celebi D, Ozkurt Z, Akcan MN (2005) Prevalence of metallo-beta-lactamase among Pseudomonas aeruginosa and Acinetobacter baumannii isolated from burn wounds and in vitro activities of antibiotic combinations against these isolates. Burns 31:707–710
61. Kanamori H, Parobek CM, Juliano JJ, van Duin D, Cairns BA, Weber DJ, Rutala WA (2017) A prolonged outbreak of KPC-3-producing Enterobacter cloacae and Klebsiella pneumoniae driven by multiple mechanisms of resistance transmission at a large academic burn center. Antimicrob Agents Chemother 61:16
62. Rosenberger LH, Hranjec T, Polliaio AD, Swenson BR, Metzger R, Bonatti H, Sawyer RG (2011) Effective cohorting and "superisolation" in a single intensive care unit in response to an outbreak of diverse multi-drug-resistant organisms. Surg Infect 12:345–350
63. Munoz-Price L, Zembower T, Penogonda S, Schreckenberg P, Lavin MA, Welbel S, Vais D, Baig M, Mohapatra S, Quinn JP, Weinstein RA (2010) Clinical outcomes of carbapenem-resistant Acinetobacter baumannii bloodstream infections: Study of a 2-state monoclonal outbreak. Infect Control Hosp Epidemiol 31:1057–1062
64. French CE, Coope C, Conway L, Higgins JP, McCulloch J, Okoli G, Patel BC, Oliver I (2017) Control of carbapenemase-producing Enterobacteriaceae outbreaks in acute settings: An evidence review. J Hosp Infect 95:3–45
65. Borer A, Eskira S, Natir S, Saidel-Odes L, Riesenberg K, Livshitz-Riven I, Schlaeffer F, Sherf M, Peled N (2011) A multifaceted outbreak of diverse multi-drug-resistant organisms. J Hosp Infect 79:325
66. Riven I, Schlaeffer F, Sherf M, Peled N, Bonatti H, Sawyer RG (2011) Effective cohorting and "superisolation" in a single intensive care unit in response to an outbreak of diverse multi-drug-resistant organisms. J Hosp Infect 95:136–140
67. Borer A, Eskira S, Natir S, Saidel-Odes L, Riesenberg K, Livshitz-Riven I, Schlaeffer F, Sherf M, Peled N (2011) A multifaceted intervention strategy for eradication of a hospital-wide outbreak caused by carbapenem-resistant Klebsiella pneumoniae in southern Israel. Infect Control Hosp Epidemiol 32:1158–1165
68. Enfield KB, Hsuq NN, Gosseling MF, Low DJ, Hazen KC, Toney DM, Slitt G, Zapata HJ, Cox HL, Lewis JD, Kundzins JR, Mathers AJ, Sifri CD (2014) Control of simultaneous outbreaks of carbapenemase-producing enterobacteriaceae and extensively drug-resistant Acinetobacter baumannii infection in an intensive care unit using interventions promoted in the Centers for Disease Control and Prevention 2012 carbapenemase-resistant Enterobacteriaceae toolkit. Infect Control Hosp Epidemiol 35:810–817
69. Merchant N, Smith K, Jeschke MG (2015) An ounce of prevention saves tons of lives: infection in burns. Surg Infect 16:380–387