International Journal of INFECTION CONTROL

SHORT REPORT

Burkholderia cepacia infection in the neonatal unit: a cautionary tale of contaminated EEG skin preparation

I-Ly Joanna Chua[1], Chris Blyth[1,2], Michelle Porter[1,3], Cara Minney-Smith[1], Adam Merritt[1], Brittany Brennan[1], Cristina Farrar[1], Linda Pelumbo[2], Danielle Engelbrecht[3] and Lisa Nicolaou[3]

[1]PathWest Laboratory Medicine, Western Australia; [2]Perth Children's Hospital, Western Australia; [3]King Edward Memorial Hospital, Western Australia

Abstract

Burkholderia cepacia isolated from a scalp wound of a neonate prompted investigation to identify potential sources. The same organism was isolated from numerous batches of gel used to prepare skin prior to electroencephalography (EEG), prompting a recall of this product. This case highlights the potential for contamination of equipment and products used for EEG.

Keywords: *Burkholderia cepacia*; *neonatal infection*; *product contamination*; *whole genome sequencing*; *healthcare-associated infection*

Received: 14 April 2023; Accepted: 27 July 2023; Published: 5 November 2024

A neonate developed a large shallow wound at the site of a previous subgaleal haematoma. This occurred following several investigations, including cerebral function monitoring, head ultrasound and electroencephalograms (EEGs). A pure growth of a non-lactose fermenting Gram negative bacillus was cultured. The isolate was further identified as *Burkholderia cepacia* complex (BCC) by MALDI-TOF (Matrix-Assisted Laser Desorption/Ionization-Time of Flight Mass spectrometry) using the Bruker Biotyper system (Bruker Daltonik, Germany). The isolated tested susceptible to meropenem, ceftazidime, cotrimoxazole, ciprofloxacin and minocycline. Additional samples referred for non-selective bacterial culture, fungal and mycobacteria culture excluded infections with other pathogens.

Isolation of this uncommon pathogen prompted environmental screening and a review of the equipment used. All equipment in direct contact with the neonates scalp were microbiologically screened, including ultrasound probes, EEG electrodes, hydrogel sensors and surgical skin markers. Topical preparations were also screened including water wipes, Coban bandage adhesive (3M, USA), chlorhexidine ointment, QV moisturising cream (Ego), Bactroban ointment, OptiLube ultrasound gel (Optimum Medical Limited), Elefix paste (Nihon Kohden), Nuprep Skin (Weaver and Co, USA) and Lemonprep EEG Skin (Mavidon, USA) preparation. Moistened swabs in sterile water were used to sample surfaces. Swabs and both partially used and unopened gels/preparations were inoculated on *Burkholderia cepacia* selective media (PathWest Media, Australia).

Numerous isolates of the same complex and antibiogram were identified from LemonPrep (Mavidon, USA; LN29824 [expiry; 09/2019; used on patient]; LN30236 [expiry: 09/2004]; LN30006 [expiry 12/2019] and LN30145 [03/2020]). All positive LemonPrep products were referred to the pharmaceutical laboratory at PathWest, to determine the total viable aerobic bacteria count. The product was neutralised with Dey/Engley neutralising broth prior inoculating to Tryptic Soy agar and SABC plates (PathWest Media, Australia). BCC cultured from all products were identified with MALDI-TOF mass spectrometry and quantified (ranging from LN29824: 64 colony forming units (CFU)/g to LN30236: 6.3 × 103 CFU/g). The alternative product offered by the same company; PediaPrep (LN 31130 Expiry 01/2022) also cultured >104 CFU/g of BCC.

The clinical isolate and isolates from LemonPrep (LN 29824, 30145 and 30236) and Pediaprep (LN31130) were referred for whole genome sequencing (WGS) and characterisation. BCC DNA was extracted using the Presto Mini gDNA Bacteria kit (Geneaid Biotech ltd). Library preparation was performed with the Nextera XT DNA library prep and sequenced using the Miseq Reagent V3 kit 2 × 300 cycles. Sequence assembly and

core genome single nucleotide polymorphism (cgSNP) analysis were carried out using the Nullarbor pipeline (https://github.com/tseeman/nullarbor). A sample from this investigation was assembled using Unicycler (https://github.com/rrwick/Unicycler) and used as the reference sequence for the pipeline. The whole genome analysis identified these isolates as Burkholderia contaminans/lata MLST Sequence Type 535 within the Taxon K *Burkholderia cepacia* complex. The cgSNP analysis showed the clinical isolate and the three LemonPrep isolates to be 0–1 SNP apart, indicating that these isolates are highly likely to be related. The Pediaprep isolate was 11–12 SNPs from the clinical isolate and LemonPrep isolates.

No other cases were identified in the hospital as a result of this contamination.

Discussion

BCC is ubiquitous and can survive in nutritionally poor aqueous environments (1). The isolation of BCC from clinical specimens from non-cystic fibrosis patients usually suggests an environmental source of infection. Approximately three-quarters of healthcare-associated *Burkholderia cepacia* (BCC) outbreaks can be traced back to an identifiable source, and more than half of them have been linked to contaminated medical products (2, 3). Surveys by the US Food and Drug Administration (FDA) and European commission indicate BCC as one of the leading causes of pharmaceutical and non-food product recalls (4, 5). Healthcare-associated outbreaks have been described from many pharmaceutical products, including ultrasound gels, mouth wash, saline flush syringes and chlorhexidine solutions (2, 3). Other common bacteria associated with commercial and pharmaceutical product contamination include Pseudomonas species, Enterobacteriaceae and Ralstonia (4, 5).

Neonate intensive care unit (NICU) patients are often premature, requiring ventilatory support and susceptible to infections. Two NICU outbreaks off BCC blood stream infections in India and Malaysia reported a mortality rate of 16 and 6%, respectively (6, 7). Risk factors associated with BCC BSI were associated with the use of long lines. Infections caused by this organism are difficult to treat as they are intrinsically resistant to first line antibiotics, including penicillins, first and second generation cephalosporins, aminoglycosides and polymyxin (2). Definite source-in for the outbreak in Malaysia could not be determined but was likely associated with ventilator water traps, and the outbreak in India was traced back to multi-use intravenous 5% dextrose and normal saline for ventilator humidifier (6, 7). A NICU outbreak in Paris identified the upper surface of capped rubber stoppers of a commercial lipid emulsion used for parental nutrition as the source (8). Outbreaks ceased with removal of the source and infection control intervention like single use intravenous fluids and cleaning of ventilatory circuits.

There are 20 species within the BCC, and closely related species in the BCC are difficult to identify using conventional biochemical and phenotypic methods. A combination of phenotypic and genotypic test is required to identify BCC species accurately. The MALDI-TOF MS can identify BCC from other gram negative non-fermenters, but BCC species identification requires further evaluation (1, 9). Currently, in our laboratory, the identification of BCC by MALDI-TOF spectrometry is supplemented by a Rec A gene analysis. The Rec A gene, which is 1,040 bp length, shows 94–95% similarity between different BCC species and 98–99% similarity within BCC species. RecA phylogeny analysis demonstrated that these isolates belong to Taxon K *Burkholderia cepacia* complex. The Rec A gene sequence is not enough to differentiate between the species of BCC in taxon K (1).

Pulse field gel electrophoresis has been the most common typing method used to characterise previous BCC outbreaks (2). In this case, WGS with cgSNP analysis has been utilised to demonstrate the relationship of the BCC isolate of the product with the patient. The isolates from LemonPrep chosen for WGS were representative of the BCC used on patient's head (LN29824), multi-stock contamination (LN30145) and the historical presence of the contamination (LN30236). BCC isolates from the three different batches of LemonPrep and the patient were highly related by cgSNP analysis, which confirmed that the BCC from the patient and product was identical and is likely secondary to a contamination at the point of manufacture. The Pediaprep was also likely related to the LemonPreps by cgSNP analysis.

The Therapeutic Goods Administration (TGA, Australia's regulatory authority for therapeutic goods) and the company were notified of the product contamination. An official worldwide product recall was initiated on 26th September 2019 of LemonPrep tubes and single use cups (10). The FDA published on 8 January 2020 that the contamination extended to additional Mavidon product including Cardio Prep and Wave Prep (11).

A number of issues were identified as a result of this investigation highlighting the potential of future risk. The LemonPrep product is used as an abrasive skin preparation lotion containing pumice intended to lower skin impedance and enhance the signal quality at the electrode site. The product specification sheet cautions the use of it in neonates, yet use of such preparations is common in practice (12). LemonPrep (and many other similar products) was produced in multi-use 4 oz (113 g) tubes as well as single use cups. The use of multi-use tubes of skin preparation increases the risk of further contamination once opened and the potential for cross transmission of infecting pathogens between patients. Reusable EEG

Citation: Int J Infect Control 2024, **20**: 23528 – http://dx.doi.org/10.3396/ijic.v20.23528

electrodes and wires are used despite challenges with reprocessing and high-level disinfection (REF). Single use EEG electrodes and vials of skin preparation should be recommended, particularly in critically unwell or susceptible individuals including neonates.

This study highlights the importance of recognising *Burkholderia cepacia* as an unusual cause of infections in neonates. This case also serves as a reminder of how potential breakdowns in production and quality of medical products can become a cause for infections and the need for stricter regulation. Appropriately and timely investigation and interventions identified EEG skin preparation as the source of infection. Despite the recall of contaminated preparations, a high degree of awareness and single-use products are recommended.

Conflict of interest and funding

This research did not receive any external funding. All work was supported by the resources of the institutions involved.

References

1. Vandamme P, Dawyndt P. Classification and identification of the Burkholderia cepacia complex: past, present and future. Syst Appl Microbiol. 2011 Apr 1; 34(2): 87–95. doi: 10.1016/j.syapm.2010.10.002
2. Häfliger E, Atkinson A, Marschall J. Systematic review of healthcare-associated Burkholderia cepacia complex outbreaks: presentation, causes and outbreak control. Infect Prevent Pract. 2020 Sep 1; 2(3): 100082. doi: 10.1016/j.infpip.2020.100082
3. Shaban RZ, Sotomayor-Castillo C, Nahidi S, Li C, Macbeth D, Mitchell BG, et al. Global burden, point sources, and outbreak management of healthcare-associated Burkholderia cepacia infections: an integrative review. Infect Control Hosp Epidemiol. 2020 Jul; 41(7): 777–83. doi: 10.1017/ice.2020.184
4. Cunningham-Oakes E, Weiser R, Pointon T, Mahenthiralingam E. Understanding the challenges of non-food industrial product contamination. FEMS Microbiol Lett. 2019 Dec; 366(23): fnaa010. doi: 10.1093/femsle/fnaa010
5. Dao H, Lakhani P, Police A, Kallakunta V, Ajjarapu SS, Wu KW, et al. Microbial stability of pharmaceutical and cosmetic products. Aaps Pharmscitech. 2018 Jan 1; 19(1): 60–78. doi: 10.1208/s12249-017-0875-1
6. Lee JK. Two outbreaks of Burkholderia cepacia nosocomial infection in a neonatal intensive care unit. J Paediatr Child Health. 2008 Jan; 44(1–2): 62–6. doi: 10.1111/j.1440-1754.2007.01173.x
7. Paul LM, Hegde A, Pai T, Shetty S, Baliga S, Shenoy S. An outbreak of Burkholderia cepacia bacteremia in a neonatal intensive care unit. Indian J Pediatr. 2016 Apr 1; 83(4): 285–8. doi: 10.1007/s12098-015-1855-7
8. Doit C, Loukil C, Simon AM, Ferroni A, Fontan JE, Bonacorsi S, et al. Outbreak of Burkholderia cepacia bacteremia in a pediatric hospital due to contamination of lipid emulsion stoppers. J Clin Microbiol. 2004 May 1; 42(5): 2227–30. doi: 10.1128/JCM.42.5.2227-2230.2004
9. Depoorter E, De Canck E, Peeters C, Wieme AD, Cnockaert M, Zlosnik JE, et al. Burkholderia cepacia complex taxon K: where to split? Front Microbiol. 2020 Jul 14; 11: 1594. doi: 10.3389/fmicb.2020.01594
10. FDA. Mavidon issues voluntary worldwide recall of LemonPrep tubes and single use cups. 2019. 2020 Dec 28;10-12: Available from: https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/mavidon-issues-voluntary-worldwide-recall-lemonprepr-tubes-and-single-use-cups [cited 28 December 2020].
11. FDA. Mavidon issues voluntary worldwide recall of manufactured products including Lemonprep tubes and single use cups Pediaprep tubes and single use cups Wave Prep tubes and single use cups Cardio prep single use cups due To Burkholderia cepacia contamination. 2019. Available from: https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/mavidon-issues-voluntary-worldwide-recall-manufactured-products-including-lemonprepr-tubes-and [cited 28 December 2020].
12. Mavidon Medical Products. LemonPrep. 2016. Available from: https://www.mavidon.com/upload/product/files/52/LemonPrep_Spec_Sheet.pdf [cited 28 December 2020].