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REVIEW

Investigation of an outbreak of *Enterobacter cloacae* in a neonatal unit and review of the literature

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KEYWORDS
Enterobacter cloacae; Neonate; Sepsis; Outbreak

Summary *Enterobacter cloacae* has emerged as an important pathogen in neonatal units, with several outbreaks of infection being reported. The aim of this study was to investigate an outbreak of sepsis due to *E. cloacae* in a neonatal unit and to review the literature. A retrospective cohort study was conducted in which cases were compared with all newborns hospitalised for more than 48 h in the neonatal intensive care unit (NICU). Cohorting of infected patients and work reorganisation were implemented. Pulsed-field gel electrophoresis was performed. The retrospective cohort included the six cases and 13 control patients that had been in the NICU during April 2006. Univariate analysis showed that the use of dobutamine was significantly associated with infection ($P = 0.036$) and that enteral feeding was a protective factor ($P = 0.02$). Multivariate analysis did not find any independent risk factor. Bed occupancy rate in March 2006 was 109.6%, indicating overcrowding. PFGE identified indistinguishable patterns among isolates from all six newborns. PubMed and OVID was search from 1 January 1983 to 15 January 2008 for papers including the terms '*E. cloacae*', 'outbreaks', 'clusters' in combination with 'neonate', 'newborn', and 'infant'.We found 26 reports of outbreaks due to *E. cloacae* in neonate patients: sixteen (52%) were bloodstream infection outbreaks, of which two (12.5%) were related to multiple-dose medications. The source for

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our outbreak was not identified. Reinforcement of hygiene practices, restrictions on new admissions and the establishment of single-dose medications helped to control the outbreak.

Introduction

In recent years, *Enterobacter cloacae* has emerged as an important nosocomial pathogen in neonatal units, with several outbreaks of infection being reported.[1–13] This agent may be transmitted to neonates through contaminated intravenous fluids, total parenteral nutrition solutions and medical equipment.[3,6,10] Many single-clone outbreaks probably caused by cross-transmission via healthcare workers (HCWs) have been described, suggesting that inpatients also can act as a reservoir.[9] Overcrowding and understaffing in periods of increased workload have also been identified as causes of nosocomial outbreaks due to *Enterobacter* spp.[5,7,8]

The aim of this study was to investigate an outbreak of sepsis due to *E. cloacae* that occurred during a short period of time in a neonatal unit and to review the relevant literature.

Methods

Settings

The Hospital das Clínicas da University of São Paulo is a 2200-bed tertiary hospital in São Paulo, Brazil. The neonatal unit has an eight-bed intensive care facility, an eight-bed facility for isolated infants, a nine-bed high-risk unit, a 15-bed intermediate-risk unit and a 23-bed low-risk unit.

Definition of cases

A case patient was defined as any newborn hospitalised in the neonatal unit in April, 2006, with positive blood culture or positive central venous catheter culture for *Enterobacter cloacae* and symptoms and signs of sepsis (fever/hypothermia, hypoperfusion/shock, hypoactivity, gastric residues, respiratory failure, leucocytosis with shift to left).

Comparative studies

To determine whether an outbreak was occurring, we compared the rates of bloodstream infection (BSI) due to *E. cloacae* before the epidemic period (from 2004 to 2006) with those occurring during April 2006.

A retrospective cohort study was conducted in which cases were compared with all newborns hospitalised for more than 48 h in the neonate intensive care unit (NICU) from 1 April to 20 April 2006. All medical records from cases and controls were reviewed to determine patients' characteristics and potential risk factors. Every prescription from every patient was reviewed and the amount of every intravenous solution administered was quantified (in mL or mg) and compared between cases and controls. Mortality of cases was attributed to *E. cloacae* BSI when no other cause had been identified.

As the hypothesis of an exogenous source was made, samples from neonatal incubators, antiseptics, alcohol solutions, povidine solutions, aliquots of opened intravenous medications, saline solutions, parenteral nutrition solutions and neonatal surfactants were collected for microbiological evaluation.

Clinical cultures

The identification and antibiotic susceptibilities of the micro-organism isolated from clinical cultures were determined using the Vitek system (bioMérieux, Marcy l'Etoile, France). The susceptibility testing was confirmed using Kirby–Bauer disc diffusion according to the Clinical and Laboratory Standards Institute.

Environmental and medication cultures

Samples of incubators were obtained by moistening cotton swabs in saline and swabbing the surface of the incubator. The swab was placed in tryptic soy broth (TSB), incubated at 35 °C, examined at 24, 48 and 72 h for turbidity.

The samples of several medications were sent to a reference laboratory. They were filtered and the filter seeded into several media including selective media with antibiotic. API 20 NE (bioMérieux) was used to identify the micro-organisms.

Infection control measures

The practices of HCWs were observed. Infection control procedures in the unit were reviewed and personnel urged to comply with these measures.