

ORIGINAL ARTICLE

Outbreak of *Pantoea agglomerans* associated with contaminated parenteral nutrition in a Neonatal Intensive Care Unit

Surto de Pantoea agglomerans associado à nutrição parenteral contaminada em uma Unidade de Terapia Intensiva Neonatal

Brote de Pantoea agglomerans asociado con nutrición parenteral contaminada en una unidad de cuidados intensivos neonatales

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ABSTRACT

Background: Contamination in the Parenteral Nutrition (PN) has been causing sepsis outbreaks. **Objectives:** The aim of this study was to describe an outbreak of *Pantoea agglomerans* detected during an epidemiological surveillance that was made in the unit, due to contaminated total parenteral nutrition in a Neonatal Intensive Care Unit (NICU) of a tertiary care hospital. **Methods:** The study was conducted in the NICU of the Uberlândia University Hospital, Brazil. It was made a surveillance in the unit collecting clinical and epidemiological data from neonates hospitalized from January 2013 to December 2016. All Bacteriologic testing including clinical, parenteral nutrition, environmental samples and hand cultures was performed and microorganisms was identified by using automated biochemical identification system (Vitek 2; bioMérieux). **Results:** In the first year of the study, an outbreak of bloodstream infection was verified. The cause of this outbreak was contaminated parenteral nutrition. The administration

of PN was discontinued immediately. All neonates affected had been born prematurely, with gestational age less than 40 weeks. There were no deaths. **Discussion:** The time to control the outbreak was three months and each step was taken to avoid the recurrence of this outbreak through epidemiological surveillance, which is extremely important for the detection of outbreaks and risk of infection factors.

Keywords: Disease Outbreaks, *Pantoea*, Parenteral Nutrition, Epidemiological Monitoring.

RESUMO

Justificativa: A contaminação na Nutrição Parenteral (NP) tem causado surtos de sepse. **Objetivos:** O objetivo deste estudo foi descrever um surto de *Pantoea agglomerans* detectado durante uma vigilância epidemiológica realizada na unidade, devido à nutrição parenteral total contaminada em uma Unidade de Terapia Intensiva Neonatal (UTIN) de um

hospital terciário. **Métodos:** O estudo foi realizado na UTIN do Hospital Universitário de Uberlândia, Brasil. Foi realizada uma vigilância na unidade de coleta de dados clínicos e epidemiológicos de neonatos internados de janeiro de 2013 a dezembro de 2016. Todos os testes bacteriológicos incluindo nutrição clínica, parenteral, amostras ambientais e culturas de mão foram realizadas e identificados microrganismos através de sistema de identificação bioquímica automatizada (Vitek 2; bioMérieux). **Resultados:** No primeiro ano do estudo, um surto de infecção da corrente sanguínea foi verificado. A causa deste surto foi à nutrição parenteral contaminada. A administração de NP foi descontinuada imediatamente. Todos os neonatos afetados nasceram prematuramente, com idade gestacional menor que 40 semanas. Não houve mortes. **Discussão:** O tempo para controlar o surto foi de três meses e cada passo foi dado para evitar a recorrência deste surto através da vigilância epidemiológica, que é extremamente importante para a detecção de surtos e risco de fatores infecciosos.

Palavras-chave: Surtos de Doenças, *Pantoea*, Nutrição Parenteral, Monitoramento Epidemiológico.

RESUMEN

Antecedentes: Contaminación en la Parenteral de la nutrición (PN) se ha producido sepsis brote. **Objetivos:** El objetivo de este estudio fue describir un brote de *Pantoea agglomerans* detectado durante una vigilancia epidemiológica que se produjo en la unidad, debido a la contaminación total de la nutrición parenteral en la Unidad de cuidados intensivos de la unidad de cuidados intensivos (NICU) de un hospital hospitalario. **Métodos:** El estudio fue conducido en la NICU de la Universidad de Uberlândia Hospital, Brazil. Se realizó una vigilancia en la unidad de ensayo clínica y epidemiológica de los neonatos hospitalizados de enero de 2013 a diciembre de 2016. All Bacteriologic testing incluyendo la clínica, la preservación de la colonización, las muestras de muestras y los microorganismos fueron identificados por el sistema de diagnóstico biológico Vitek 2, bioMérieux). **Resultados:** En el primer año del estudio, se produjo un brote de la circulación sanguínea. La causa de este brote se ha contaminado la preservación de la nutrición. La administración del PN ha sido discontinued inmediatamente. Todos los recién nacidos afectados han sido post prematurely, con gestational age less than 40 weeks. En el momento. **Discussión:** El tiempo para controlar el brote fue de tres meses y cada paso fue para evitar los recurrentes de este brote a través de la vigilancia epidemiológica, que es muy importante para la detección de brotes y los riesgos de factores de deterioro.

Palabras clave: Brotes de Enfermedades, *Pantoea*, Nutrición Parenteral, Monitoreo Epidemiológico.

INTRODUCTION

The first Neonatal Intensive Care Unit (NICU) was implemented in 1960 and since then the rate of neonatal mortality has fallen than 4-fold. This decline can be attributed to the highly specialized care provided to premature and sick infants by neonatologists and multidisciplinary teams working in NICU.¹

The high risk of infection in neonates are lower gestational age, immature immune system as well as the use of invasive procedures like Central Venous Catheters (CVC), intravenous administration of medications and Parenteral Nutrition (PN). Surveillance is the best way to control infections in intensive care unit.²

Contamination in the PN has been causing sepsis

outbreaks. This contamination is the result of errors in the composition of PN in the pharmacy and manipulation done incorrectly in the ward. Contamination on parenteral nutrition prepared by compounding pharmacy was described by Gupta et al. (2014), that included 5 patients presenting *Serratia marcescens* bloodstream infections. Another report included an outbreak occurred in the neonatal pediatric unit due to contamination of parenteral nutrition in a Medical School Hospital in Turkey.³⁻⁵

Pantoea agglomerans known as *Erwinia herbicola* and *Enterobacter agglomerans*, is a facultative anaerobic gram-negative bacillus that has been isolated from the blood in the context of outbreaks caused by the use of contaminated intravenous products. Between 1st of January 1994 and 1st of June 2005, 125 of 6383 patients (2%) in a 24-bed level III NICU became colonized with *Pantoea agglomerans*. Three newborns exhibited late-onset *Pantoea agglomerans* septicemia and died.^{6,7}

The objective of this study is describe an outbreak of *Pantoea agglomerans* detected during an epidemiological surveillance that was made in the unit, due to contaminated total parenteral nutrition in a NICU of a tertiary care hospital.

METHODOLOGY

The study was conducted in the NICU of the Uberlândia University Hospital, Brazil. The unit has 15 beds, rated level 3, and admits an average of 350 infants each year. It was made a surveillance in the unit collecting clinical and epidemiological data from neonates hospitalized from January 2013 to December 2016. The surveillance was carried out in accordance to the *National Healthcare Safety Network (NHSN)*.

NHSN was created in 2005 with the purpose of estimating an occurrence of cycles associated with health as well as to make a shielding of the same, to facilitate an interface of comparisons of risk of each hospital so that it takes steps and assistants in the development in the hospital and an application of control measures.⁸

The following data were extracted from studies meeting inclusion clinical and infection data: birth weight, reason for hospitalization, use of invasive devices, parenteral nutrition, mechanical ventilation, drain and phlebotomy, need surgeries, length of hospitalization, microorganism, antimicrobial use and infection site. Specimens for culture were collected based on clinical criteria established by the medical staff. Microbiological data were obtained from the Microbiology Laboratory of the Uberlândia University Hospital.

An Nosocomial Infection (NI) was defined as an infection not present or incubating when the patient is admitted to hospital or other health care facility at the time of NICU admission, with onset after 48h of stay.⁹

An infection is defined as bloodstream infection at least one of the following criteria: One or more positive blood cultures by micro-organisms that do not contaminate the skin and that the microorganism is not related to infection elsewhere; At least one of the signs and symptoms: thermal instability, apnea, bradycardia, food intolerance, worsening of respiratory distress, glucose intolerance, hemodynamic instability or hypoactivity.¹⁰

During September to November 2013, eight neonates were diagnosed with *Pantoea agglomerans* in bloodstream infection that had no such infections in the previous year. The infected patients developed infections while receiving a parenteral nutrition. This outbreak occurred in the NICU of a tertiary teaching Hospital in Brazil and was the first outbreak by *Pantoea agglomerans* due to parenteral nutrition contaminated in unit and all hospital. The batch of parenteral nutrition

in unit are outsourced, therefore the contamination is resulted from errors during compounding. On November 2013, the unit stopped using the product and sent a batch of unopened parenteral nutrition to analysis. Additionally, environmental samples from unit were collected included swab samples of high-touch surfaces in the infusion bomb, faucet and drain of each sink. Hand cultures were obtained from healthcare professionals.

All Bacteriologic testing including clinical, parenteral nutrition, environmental samples and hand cultures was performed and microorganisms was identified by using automated biochemical identification system (Vitek 2; bioMérieux).

For the outbreak detection, only univariate logistic regression was used. The tests were performed using SPSS software v.2.0.

This research was approved by the Committee of Ethics in Research with Human Beings of the Federal University of Uberlândia with the opinion n 1.776.703. This research followed the recommendations of Resolution CNS 466/12 and complied with the ethical principles contained in the Declaration of Helsinki 2008 of the World Medical Association.

RESULTS

The surveillance was extended for four years, from January 2013 to December 2016. In the first year of the study, an outbreak of bloodstream infection was verified. The initial identification by conventional biochemical reaction showed positive blood culture for *Pantoea agglomerans*. Eight neonates were infected as shown in figure 1.

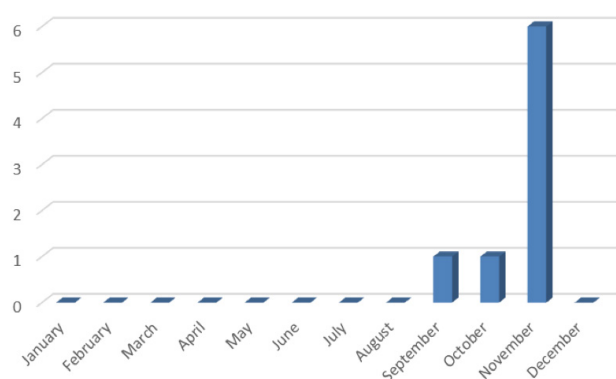


Figure 1. Outbreak caused by *Pantoea agglomerans* in September to November of 2013 in NICU of HC-UFU.

All neonates affected had been born prematurely, with gestational age less than 40 weeks. Six neonates were very low birth weight (VLBW) and all were on parenteral nutrition. There were no deaths (Table 1).

The cause of this outbreak was contaminated parenteral nutrition. Since two babies developed signs of septicaemia in a short time, a common source such as PN was suspected. On November 2013, the unit sent a batch of unopened parenteral nutrition to analysis and the result showed growth of *Pantoea agglomerans*. The usage of PN was stopped temporarily for all neonates. All staff involved in the care of babies, pharmacy staff and the infection control team were alerted to the outbreak. The affected neonates were cohorted, and dedicated instruments were assigned to each neonate. The importance of strict handwashing practice was re-emphasized among staff. Based on the rapid deterioration of the neonates, Gram-negative sepsis was suspected and, therefore, the babies were put on treatment with intravenous imipenem.

No other neonates in the NICU were infected or colonized by this microorganism. Environmental samples from unit and hand cultures from healthcare professionals were negative for *Pantoea agglomerans*.

DISCUSSION

This study describes a bloodstream infection outbreak by *Pantoea agglomerans* occurred in September to November 2013. This is the first outbreak caused by this bacteria in the unit, as well as throughout the hospital, as a result contaminated parenteral nutrition with eight infected neonates in 2013.

Pantoea agglomerans are Gram negative opportunistic pathogens that infect vulnerable immune system patients. It's primarily an environmental and agricultural organism that inhabits plants, soil and water, causing urinary infections and blood sepsis. This is an unusual microorganism in the etiology of neonatal infection sepsis, but mainly *Pantoea agglomerans* has been associated to several outbreaks in neonatal unit.^{11,12} In this study, all *Pantoea agglomerans* isolated have similar phenotypical characteristics, as showed by automated biochemical identification profile and by antimicrobials susceptibility results.

Pantoea agglomerans infection in neonates in outbreaks is caused by contaminated parenteral nutrition solutions due to its ability to grow in commercial infusion fluids. Preterm neonates are highly susceptible patient group for bacterial infections and fast detection of blood sepsis and identification of the causative agent are critical to a better treatment. However, even when the microorganism has a fast detection, the infections has a bad course, causing septicemic, shock

Table 1. Clinical characteristics of the eight neonates with bloodstream infections caused by *Pantoea agglomerans*.

Neonate	Data of positive blood cultures	Weight (g)	Gestacional age (Weeks)	Antimicrobial susceptibility profile ^a	Diagnosis	Use of parenteral Nutrition	Outcome
1	30.09.13	1390	32	Sensitive	RDS ^b	Yes	Survival
2	03.10.13	1840	31	Sensitive	RDS	Yes	Survival
3	09.11.13	2200	34	Sensitive	RDS	Yes	Survival
4	11.11.13	1282	34	Sensitive	RDS	Yes	Survival
5	11.11.13	1460	29	Sensitive	RDS	Yes	Survival
6	13.11.13	1138	23	Sensitive	RDS	Yes	Survival
7	14.11.13	1060	34	Sensitive	RDS	Yes	Survival
8	14.11.13	1390	37	Sensitive	RDS	Yes	Survival

^a Amicacin, Ampicillin, Cephalothin, Cefoxitin, Cefepime, Imipenem, Etapenem, Gentamicin, Ciprofloxacin.

^b RDS, respiratory distress syndrome.

and respiratory failure. In addition, is difficult to identify this microorganism as a result of the biochemical heterogeneity of the genus *Pantoea agglomerans*.^{3,11,13,14}

A similar case of outbreak occurred one hospital of Campinas, São Paulo State, Country Brazil, notified the Municipal Secretary of Health. In that hospital, occurred an outbreak of bloodstream infection associated with contaminated parenteral nutrition by *Pantoea agglomerans*. Among 49 affected patients of this Municipality, 12 died (two adult and 10 neonates).¹⁵ In our study no one neonates was died. The NICU personal conducted a timely comprehensive outbreak investigation, stopping using the product immediately on the suspicion of contamination.

Surveillance of Nosocomial Infections (NI) is an essential part of quality patient care.¹⁶ For the effective control of infections, the hospital must have structure and maintain a system of epidemiological surveillance of NIs, especially in critical sectors such as NICU.¹⁷ The surveillance is an important and necessary component of prevention programs, enabling burden of illness, trends and the improvement initiatives to be evaluated.¹⁸ Outbreaks reported in the literature range from cases limited to colonization discovered through routine or active surveillance. The detection and investigation of an outbreak will depend mainly an active surveillance.¹⁹

In this study through surveillance, an outbreak by *Pantoea agglomerans* was detected caused by contaminated parenteral nutrition, with eight infected neonates in 2013. This control as well as intervention for NICU personal were fast and effective. Every step has been taken to prevent recurrence of the outbreak. Therefore, epidemiological surveillance becomes extremely important to detection of outbreaks and risk of factors for infection statistically significant as well as the most isolated microorganism and the most common nosocomial infection. Thus health professionals can have a direction for a better course to be followed, becoming the neonatal prognosis more positive.

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