Klebsiella pneumoniae Outbreak in a Cancer Unit of a General Hospital - Predisposing Factors and Evaluation of the Impact of Intervention Measures

Cristiane Pavanello Rodrigues Silva[1,2],
Jorge Manoel Buchdid Amarante[2],
Rúbia Aparecida Lacerda[1] and
Maria Lúcia das Neves Biancalana[2]

Nursy School of University of São Paulo[1], Samaritano Hospital[2]; São Paulo, SP, Brazil

We made a retrospective cohort study of a primary bloodstream infection outbreak in patients of a cancer unit in a general hospital, evaluated the impact of intervention measures and investigated the predisposing factors. The targeted predisposing factors were selected based on the medical literature. The data were treated with univariate analysis to calculate the relative risk, and statistical significance was set at p<0.05. The presence of a long-term totally-implanted central venous catheter appears to be a predisposing factor, while a peripheral venous catheter appears to have offered protection from infection. This is reinforced by fact that intervention measures controlled the outbreak, suggesting cross-contamination from a common source. These findings corroborate the fundamental role of the hospital infection control service in early intervention and reinforce the need for continued training of health professionals that perform this type of care.
<u>Key Words</u>: Nosocomial infection, hospital-acquired infection.

Hospital Infection Outbreaks

One of the greatest challenges for a Hospital Infection Control Service (HICS) is the identification and control of outbreaks of hospital infections (HI), which generally are identified by epidemiological surveillance (ES) and by an active search for HI cases. According to Grinbaum (2000) [1], "one of the objectives of ES carried out by the HICS is to detect outbreaks before the propagation results in further harm."

In addition to outbreak control intervention activities, the HICS is also charged with investigating the source of the agent and the means of transmission. Usually HIs are a result of an imbalance between the patient's defense mechanisms and microbiota. The most common

route of transmission of nosocomial pathogens is on the hands of the care team; however, other potential sources are water, fomites, instruments and solutions. Invasion by these agents is most likely to occur due to poor aseptic techniques, failure of environment cleaning measures, inefficient hand washing, ineffective material sterilization processes, etc. [2].

When an outbreak occurs, the HICS should establish an investigation protocol, and although this protocol cannot always be followed in an exact order, owing to the urgency of intervention measures, it should include an investigation of the patient, the environment and the agent, in order to establish possible risk factors for further investigation, and to prove or disprove the hypotheses that are developed. The investigation of the outbreak of an infectious disease should consist of the following steps [3]: 1) establish a case definition; 2) make a diagnosis and check the veracity of other "cases"; 3) determine if an epidemic exists, based on the number of confirmed cases and on prior occurrence of the disease; 4) define the objective of the investigation; 5) analyze the data available with regard to characteristics of time, space and people; 6) develop

hypotheses; 7) test hypotheses; 8) evaluate the prevention and/or control measures; 9) communicate the results of analysis to all interested parties.

Description of an Outbreak of *Klebsiella pneumoniae* in an Adult Patient Cancer Unit

Initially, two cases of primary bloodstream infection (BSI) by *K. pneumoniae* were diagnosed in December 2002 in the adult cancer unit of a private general hospital in the city of São Paulo. These cases, by themselves, were not considered exceptional for this unit; however, within a month, in January of 2003, five more cases and one more related to a peripheral venous catheter (PVC) appeared, for a total of eight cases with the same topography, the same agent, in the same environment and in the same population. In addition to the classic signs and symptoms of bacteremia, these cases were diagnosed by culturing two pairs of central- and peripheral-blood samples from each patient.

The pattern of cases indicated a possible exposure of this patient population to an infectious agent. The cases appeared in rapid succession and then declined rapidly, suggesting a common source of infection and a short interval of exposure [3].

The HICS acted to confirm the occurrence of the outbreak, carried out intervention actions for its control and investigated the predisposing cause(s). After the introduction of intervention measures, only two contaminated patients were detected in February 2003, for a total of 10 cases (seven BSI by central venous catheter (CVC), one BSI by PVC and two colonized). The objectives of our study were: 1) to evaluate the impact of the intervention measures to control an outbreak of *K. pneumoniae* in an adult cancer unit in a private general hospital; and 2) to discover the predisposing causes for the occurrence of this outbreak.

Material and Methods

This retrospective cohort study was conducted from December 2002 to February 2003 in an adult cancer unit in a medium-sized private general hospital in the city of São Paulo. The population under investigation for predisposing causes consisted of 20 hospitalized patients in this unit over this period. Among these patients, 10 had been contaminated (eight presented BSI related to CVC and PVC and two had been colonized by the infectious agent). The other 10 (non-cases), which did not present *K. pneumoniae* infection or colonization, had been hospitalized in the same unit and for the same period. It was not possible to carry out molecular typing; however, all of the positive blood culture samples and/or perianal swabs had the same phenotypic antibiogram profile; all the samples were only resistant to ampicillin.

Initially, the following intervention measures were introduced to control the outbreak: 1) identification of the bacteremia cases; 2) identification of colonized patients by weekly perianal swab cultures from all of the patients in the unit; 3) contact isolation- segregation of infected and colonized patients (division of the professional team for provision of care); 4) alcohol gel in individual containers for antisepsis of the hands; 5) special care in vascular access (re-training for antisepsis and bandaging); 6) hand washing.

An investigation into the predisposing causes was initiated, using computer patient charts as the data source. A number of predisposing factors were selected, based on the scientific literature [4-6]. These factors were judged most relevant to this patient population: 1) presence of neutropenia; 2) type of vascular access (as all of the patients had vascular access); 3) duration of vascular access; 4) presence of a central and/or peripheral venous catheter; 5) parenteral nutrition during the outbreak; 6) blood derivatives administered during the outbreak; 7) duration of stay in the intensive care unit (ICU); 8) presence in the operating room; 9) use of a nebulizer or vaporizer during the outbreak.

The base pathology, hospitalization stay and vascular insertion point were also indicated in the literature, but they were not evaluated because the patients all presented the same pathology (cancer), a similar mean time of hospitalization, which varied from five to nine days, and the same insertion point for the CVC (subclavian vein).

A spreadsheet was created, containing patient identification, duration of hospitalization, blood culture and anal swab results, as well as the other selected predisposing factors. Univariate analysis was done for each factor, and the Epi-Info version 6.04 statistical program was employed. The Mantel-Haenszel chi-square test was used to evaluate the statistical significance of association (p).

Results

After the adoption of the intervention measures, only two cases of colonization were detected in February of 2003. From then until August 2003, no other case of infection or colonization was detected in the cancer unit. This indicates that the interventions that were adopted controlled the outbreak and broke the transmission chain. A fall in the incidence of HI related to the CVC was also observed when compared with indices prior to the outbreak.

The results of the investigation into predisposing factors are presented in Tables 1 and 2.

Among the factors considered, exposure to a totally implanted CVC (Port-A-Cath type) resulted in an approximately four times greater risk for the occurrence of the infectious event (RR = 3.86 and p = 0.057). A PVC may have helped protect against BSI in those patients who used them, with or without simultaneous CVC use (RR = 0.26 and p = 0.057). The confidence interval of 95% for these associations showed the values to be at the limit of statistical significance, most probably due to the limited number of cases.

According to Waldman (2000) [3], who discussed the limitations of such studies: "despite the fact that investigations of outbreaks are an important instrument for health services, we must point out a few of their limitations, which include: a) it is generally not possible to use well-planned research protocols; b) it is frequently an investigation that uses different sources of information, which can vary dramatically in completeness and accuracy, as does the purpose with which they were originally recorded; c) unlike planned studies, in which the size of the sample is properly

established by epidemiologists, with investigations into outbreaks the number of cases is generally small, which makes the analysis of a number of aspects difficult."

In an effort to determine if there was a relationship between the event and CVC use, the duration of use was analyzed. It was observed that more than half of the CVC (73%) had been implanted in the patients for more than 30 days. The mean duration for the (infected) cases was far longer (348 days) than for the non-cases (64 days).

Discussion

The agent involved, *K. pneumoniae*, is part of the respiratory and intestinal microbiota of humans and is isolated from the oropharyngeal cavity at a frequency of 1 to 6% [7]. It is strongly associated with infections, such as pneumonia, urinary infections and septicemias, since the hospital environment is associated with long-term hospitalized patients and/or those who have been in the ICU, mainly those submitted to oropharyngeal intubation, for which the hand of the health worker is the main vehicle for the spread of the agent among the hospitalized patients [8]. Between half and three-quarters of all the bacteremias caused by this agent originate in the hospital; therefore they are resistant to ampicillin and carbenicillin, and are frequently susceptible to cephalosporins, cotrimoxazole, aminoglycosides and imipenem [9]. This pattern was also found in our study, as the HI cases were caused by ampicillin-resistant *K. pneumoniae*.

Primary bacteremias can occur without apparent infectious sources, however there is often an association of disease with mechanisms for access to the vascular system. In the hospital environment, vascular access and contaminated intravenous infusions are often involved. Most of these infections occur in the ICU and in other units for the treatment of seriously ill patients [10].

Every patient in this study had a mechanism for vascular access and most of the BSI cases occurred in those with long-term CVC, of the Port-A-Cath type, already punctured and the only access in use.

Table 1. Predisposing factors, relative risk (RR) and statistical significance for blood stream infection by *Klebsiella pneumoniae*

Predisposing factors	Cases		Non-Cases		RR	P	CI 95%
	Exp.	Not exp.	Exp.	Not exp.			
Neutropenia	3	7	2	8	1.29	0.61	0.52-3.15
Port-A-Cath	9	1	5	5	3.86	0.057	0.62-24.08
Hickman	0	0	1	9	0	0	0
Long-term parenteral nutrition	0	0	2	8	0	0	0
ICU	0	0	2	8	0	0	0
Surgical center	2	8	2	8	1	1	0.33-2.99
Peripheral venous catheter	1	9	5	5	0.26	0.057	0.04-1.62
Blood derivatives	0	0	4	6	0	0	0
Vaporizer/nebulizer	1	9	2	8	0.63	0.54	0.12-3.32

P: probability; CI: confidence interval; Exp.: exposed; ICU: intensive care unit.

Table 2. Duration of central catheter use in cases and non-cases of bloodstream infection

Duration (days)	Cases		Non-Cases		Total	
	N	%	N	%	N	%
Up to 7 days	0	0	0	0	0	0
8-30 days	2	22	2	33	4	27
>= 31 days	7	78	4	67	11	73
Total	9	100	6	100	15	100

It is well known that most BSI cases are related to CVC use. The risks rise when seriously ill patients are grouped together, depending on the type of disease (immunodepression), whenever there are irregular insertion conditions (elective vs. urgent), and depending on the type of catheter (tunneled *vs.* non-tunneled or subclavian *vs.* jugular). Catheter characteristics must also be considered, such as the polymer with which they are manufactured, as well as virulence factors of the microorganism. *In vitro* studies show that polyvinyl and polyethylene catheters are less resistant to the adherence of microbes than those made of Teflon, silicone and polyurethane [11].

The most common path of infection by short-term peripherally-inserted catheters is the migration of microorganisms from the skin to the point of insertion. In long-term catheters, contamination from the catheter connection contributes substantially to intraluminar colonization. Occasionally, catheters can become hematogenically contaminated, and, less often,

contamination may occur from intravenous infusion. The point at which the catheter is inserted also influences the subsequent risk of infection [11].

An implanted catheter is a type of CVC that is implanted in a subcutaneous chamber, in the subclavicular region [10]. The Port-A-Cath type is made of silicone or tunneled polyurethane and a reservoir, generally made of titanium, with a silicone membrane, which makes multiple punctures possible. It is implanted in the subcutaneous tissue with a chamber that secures it in place and which facilitates puncture with a special needle. It is a long-term (approximately five years) catheter and is associated with a low risk of blood stream infection (0.21 episodes/1000 days of catheter), when compared with other tunneled catheters (2.77 episodes/1000 days) [12,13].

The infections found in our study were mainly related to long-term CVC use. The determining factor in this association may be the greater number of punctures in the cases than in the non-cases, since the mean duration of catheter use for the cases was 348 days, while it was 64 days for the non-cases. The occurrence of an outbreak caused by a single microorganism suggests a common exogenous contamination source, probably due to carelessness. Except for one case, all the patients had a CVC as the only means of access to the vascular system. This is reinforced by the suggestion that the PVC appeared to serve as a protective factor, since it receives less manipulation than the CVC and therefore presents a lower risk of contamination.

Conclusions

Although the Port-A-Cath type CVC may have been a predisposing factor for BSI, it alone was not responsible for the occurrence of this outbreak. The determining factor of the outbreak appears to have been carelessness in handling during care procedures, since after the review of intervention measure techniques and retraining of hand hygiene, the outbreak was controlled. Although the reservoir and the source of this agent were not identified, it is clear that cross contamination was determinant for these occurrences during the care procedures, and that the hospital infection control service's continuous and permanent oversight and the training of health professionals who directly care for patients are fundamentally important.

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