Central Venous Catheter-Related Sepsis in a Cohort of 366 Hospitalised Patients

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Five hundred two central venous catheters inserted in 366 patients were evaluated prospectively over a one-year period to determine the frequency and risk factors associated with catheter-related sepsis. For study purposes, in cases in which catheter infection was suspected but the initial blood cultures were negative, the catheters were replaced by guidewire technique; otherwise, the catheters were routinely changed after 21 days by guidewire technique. A catheter-related infection was suspected in 190 cases (190/502, 38%). A diagnosis of catheter-related sepsis was established in 50 patients, which represents 10% of the total number of lines (502). Over a total of 6428 days of catheter use, the infection rate was 0.8 cases of sepsis per 100 catheter-days. Staphylococcus epidermidis, Staphylococcus aureus, and Candida spp. were the most frequently isolated aetiological agents of sepsis. On univariate analysis, six variables affecting the rate of catheter-related sepsis were identified: neutropenia for more than eight days (p < 0.001); AIDS (p < 0.001); haematological malignancy (p < 0.001); administration of total parenteral nutrition (p = 0.001); duration of site use (p = 0.04); and high APACHE II score (p = 0.04). The logistic regression analysis revealed that AIDS and haematological malignancies were independent risk factors of catheter-related sepsis. Catheter replacement over a guidewire was no more likely to be associated with sepsis than was percutaneous catheter insertion. In conclusion, although the incidence of established catheter infection is much lower than the incidence of suspected infection, in most cases of suspected infection it is wise to change the catheter with the guidewire technique and wait for culture of the tip, rather than to remove the catheter immediately. Such a policy may help reduce the number of unnecessary catheter removals.

During the last several years, the management of acutely ill patients or patients requiring long-term intravenous therapy has changed because of the widespread use of central venous catheters (CVCs). The major medical complication associated with the use of intravascular devices is infection, with CVC-related sepsis being the most common, often underestimated, and frequently incorrectly managed infectious complication (1-3). Surveys from the USA report that 2 to 12% of CVCs cause sepsis, with an average of 100,000 patients affected annually (4-6). Most cases of CVC-related sepsis resolve with antibiotic therapy, often combined with catheter removal; in a minority of patients, life-threatening complications such as suppurative thrombophlebitis, endocarditis, and metastatic infections occur (7-8).

To identify the most relevant factors predisposing to CVC-related sepsis, we analysed the impact of multiple variables on the development of infections in a prospectively followed cohort of hospitalised patients with CVCs. Significant predictors of sepsis using univariate analysis were subsequently compared with a multivariate statistical model.

Patients and Methods

Patients. The study cohort comprised 366 patients requiring the insertion of a CVC who had been admitted during a one-year period (1 January to 31 December 1994) to a university hospital...
hospital in Rome, Italy, a 1500-bed regional referral centre that includes an AIDS clinic. Patients in the study were randomly selected from several medical and surgical wards, excluding intensive care units; they were chosen from 623 patients with CVCs out of the approximately 16,000 patients admitted to the hospital during the study period.

The original size of the group of randomly selected patients was 400. Twelve patients were excluded from the study because their lines were removed in the first 12 to 24 h after sepsis was suspected, before blood cultures were performed; nine patients, because the microbiology laboratory did not receive their catheters; six patients, because they did not fulfill the study's specified criteria of three blood cultures; and seven patients, because of lack of data.

A short-term polyurethane catheter (Certofix; Braun, Melsungen AG, Germany) was inserted by different surgeons on the same surgical team, using the Seldinger technique. The catheters were inserted into various sites (internal jugular, subclavian, or femoral vein) as judged most convenient by clinical evaluation. The gauze dressings were changed twice a week using the following aseptic technique: surgeons washed their hands and wore masks, sterile gowns, and gloves; the puncture site was prepared with providone-iodine solution; and surrounding areas were covered with sterile drapes. All tubings were changed every two days. Dressings and tubing were routinely changed by nurses. The medical records of all patients were reviewed by an infectious disease specialist.

Study Design. Follow-up began at the time of the insertion and ended when the CVC was removed or death occurred. Indications for catheter removal included end of treatment, suspected CVC infection, and major mechanical problems such as catheter kinking, obstruction, or leaking. In some cases of suspected infection or minor mechanical problems, the catheters were replaced by the guidewire technique; otherwise, the CVCs were routinely changed after 21 days (when the patient needed a central line for a prolonged period of time) by the guidewire technique.

In an individual without any other evident source of sepsis, criteria for suspected CVC-related sepsis were: body temperature > 38°C, purulent discharge at the skin insertion site, and systemic signs of sepsis. For all patients who exhibited one or more of these signs, at least three blood cultures were aseptically collected from peripheral veins, at not less than hourly intervals. The CVC was removed 24 to 48 h after the patient developed signs of sepsis if at least one blood culture was positive. If blood cultures were negative, the CVC (or a catheter routinely exchanged by guidewire) was simply replaced, using the guidewire technique. All lines suspected as sources of sepsis, either removed or changed via guidewire, were cultured. The new (i.e., replacement) CVC (inserted via guidewire) was removed if a culture of the tip from the previous CVC removed from the same site became positive and the patient was still febrile despite antibiotic therapy. Otherwise, the CVC remained in situ. If central venous access was still needed, a new CVC was placed at a different site.

For the purpose of this study, CVC-related sepsis was diagnosed if a catheter infection occurred in a bacteremic patient for whom cultures of both the catheter and blood yielded the same microorganism and there was no source of sepsis other than the catheter itself. The following complications confined to the insertion site were classified as local infections: phlebitis, cellulitis, and superficial abscesses.

Parameters Evaluated. For each patient the following data were collected: age, sex, underlying disease, history of intravenous drug abuse, duration of hospitalisation prior to catheter insertion, number of circulating polymorphonuclear (PMN) cells (×10⁹/l), CVC insertion site, insertion technique (direct venipuncture or guidewire replacement), date of insertion and removal, surgeons' skill and experience in insertion of CVCs, indication for CVC (i.e., chemotherapy, administration of antibiotics, parenteral nutrition), and number of catheter manipulations. In patients with CVC-related sepsis, we also analysed the interval between catheter insertion and the detection of sepsis, the aetiological agents, the management of the infection (antibiotics, catheter removal), and the outcome.

Prognosis immediately before insertion of the CVC was retrospectively assigned using the modified Horn's index (9): low (single mild illness), moderate (more severe disease but uncomplicated recovery), major (major complications or multiple conditions requiring treatment), and extreme (catastrophic illness leading to death). The revised acute physiology and chronic health evaluation were assigned by the APACHE II system (10). The length of neutropenia (i.e., circulating PMNs < 500/mm³) was counted for the duration of catheter placement.

Microbiological Analysis. Ten ml of blood, aseptically collected from patients with suspected sepsis, was inoculated (5 ml in each of 2 bottles) into Bactec vials (NR6A for aerobic culture, NR7A for anaerobic culture; Becton Dickinson, USA). All instrument-positive vials were gram stained and subcultured. Isolates were identified by microscopic examination and biochemical and serological tests.

Each catheter segment was cultured by two methods: the semiquantitative method of Maki et al. (11) and the quantitative technique developed by Cleri et al. (12). All microorganisms recovered were identified and their in vitro susceptibility to antibiotics established by standard methods.

Statistical Analysis. Differences in the means were tested for normal distribution and compared using Student's two-tailed t-test. Differences in the group proportions were assessed using the chi-square test or, for small numbers, Fisher's exact test. Potential risk factors for CVC-related sepsis were analysed by univariate methods to screen for possible inclusion into multivariate models. Ninety-five percent confidence intervals (95% CI) were used to determine the statistical significance of the relative risk (RR). Multivariate analysis was performed with logistic regression models to predict the likelihood of sepsis and determine a multivariate RR (mRR) for each factor. Two-tailed tests of significance (at the p < 0.05 level) were used to determine statistical significance. Statistical analysis was performed using the software program Egret (Statistics and Epidemiology Research, USA).

Results

Population Data. During the study period, 502 CVCs in 366 of a total of 623 patients with CVCs were investigated. Table 1 summarises the population data. Two-hundred thirty-seven (65%) patients were hospitalised in medical wards and 129 (35%) in surgical wards. The indications for CVC implantation were total parenteral nutrition (210/502, 42%), chemotherapy (202/502, 40%), antibiotic therapy (145/502, 29%), administration