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Comparison of triple-lumen central venous catheters impregnated with silver nanoparticles (AgTive®) vs conventional catheters in intensive care unit patients

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SUMMARY

Background: Silver-impregnated central venous catheters (CVCs) have been proposed as a means for preventing CVC colonization and related bloodstream infections (CRBSIs).
Aim: To evaluate the efficacy of CVCs impregnated with silver nanoparticles in a large group of critically ill patients.
Methods: A prospective, randomized clinical trial was conducted in five intensive care units (ICUs). Three hundred and thirty-eight adult patients requiring CVCs between April 2006 and November 2008 were randomized to receive AgTive silver-nanoparticle-impregnated (SC) or conventional (CC) CVCs. Primary endpoints were CVC colonization (growth of $\geq$15 colony-forming units from the catheter tip) and incident CRBSIs (meeting the definitions of the Centers for Disease Control and Prevention). Infection-free time (days from initial CVC insertion to initial blood culture positivity) and ICU mortality rates were measured as secondary endpoints.
Findings: The SC group ($N = 135$) and CC group ($N = 137$) were similar in terms of clinical and laboratory parameters at baseline, reasons for ICU admission, complications during CVC insertion, and total time with CVC (mean $\pm$ standard deviation; SC 13 $\pm$ 24 vs CC 15 $\pm$ 37 days). No significant intergroup differences were found in CVC colonization rates (SC 32.6% vs CC 30%; $P = 0.7$), CRBSI incidence rates (3.36 infections per 1000 catheter-days in both groups), infection-free times (SC 13 $\pm$ 34 vs CC 12 $\pm$ 12 days; $P = 0.85$) or ICU mortality (SC 46% vs CC 43%; $P = 0.7$).

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Conclusion: In critically ill patients, use of AgTive® silver-nanoparticle-impregnated CVCs had no significant effect on CVC colonization, CRBSI incidence or ICU mortality. These CVCs cannot be recommended as an adjunctive tool for control of CRBSIs.

Introduction

Central venous catheters (CVCs) are indispensable for managing most critical illnesses, but their use is associated with an increased risk of bloodstream infections (BSIs). In the USA, where the use of CVCs in intensive care units (ICUs) has been estimated at one million catheter-days per year, approximately 80,000 cases of CVC-related BSIs are reported annually.[1–6] Biomaterial technology has developed a number of strategies aimed at reducing these complications,[7,8] including the use of catheters coated or impregnated with anti-infective agents (e.g. antiseptics, antimicrobials, antimetabolite substances and silver ions). Studies on the efficacy of these devices have yielded conflicting results.[9–13] Silver-ion-eluting CVCs have been tested in critically ill and cardiac surgery patients, but – with rare exceptions[14,15] – the results have been unconvincing.

A newer generation of silver-impregnated CVCs (LogiCath AgTive®, MedeX Medical Inc., Naseby, Northants, UK) has been marketed with the claim of enhanced bactericidal activity. AgTive catheters are made of polyurethanes impregnated with silver nanoparticles, and their interaction with body fluids and intravenous solutions results in the release of significantly larger amounts of silver ions from the inner and outer surfaces of the catheter.[16] In a single-centre, prospective trial conducted in a mixed population of ICU and non-ICU patients, these silver nanoparticle-impregnated catheters markedly reduced CVC colonization rates and catheter-associated infection rates compared with non-antiseptic CVCs.[17] This article reports the results of a multi-centre, randomized, controlled trial to assess the efficacy of CVCs impregnated with silver nanoparticles in a large population of critically ill patients in ICUs.

Methods

Patients

Patients were recruited in the ICUs of five Italian university hospitals from April 2006 to November 2008. The study protocol was approved by the institutional review board of the coordinating centre (Università Cattolica del Sacro Cuore, Protocol No. 254 A.474/C.E./2005) on behalf of all participating centres. Adult patients ($\geq$ 18 years) scheduled to undergo central venous catheterization (via subclavian or internal jugular route) were enrolled with informed consent. Exclusion criteria were a history of unsuccessful attempts at catheterization or evidence of previous surgery, skeletal deformity and/or scarring involving the catheterization site.

Endpoints

The primary endpoints were crude CVC colonization rates and the incidence of catheter-related bloodstream infections (CRBSIs) (number of infections per 1000 catheter-days). Infection-free time (measured in days from the time of initial catheterization to the time of initial blood culture positivity) and ICU mortality rates were secondary endpoints.

CVC insertion, care and removal

All CVCs were inserted at subclavian or jugular sites in accordance with the recommendations of O'Grady *et al.*[5] The insertion site was covered with a transparent, semi-permeable dressing that was inspected daily and changed when necessary. Tubing and three-way stopcocks were changed according to local protocols or when needed. Catheters remained in place as long as required, and this need was assessed regularly. Whenever a CVC was removed (because it was no longer needed, not functioning properly or thought to be infected), the tip was submitted for semi-quantitative culture[18] and antimicrobial susceptibility studies. Blood cultures and other microbiological studies were ordered as indicated. Catheter removal was not standardized, but physicians were advised to make every effort to avoid tip contamination. Catheter exchange over a guidewire was only allowed in the absence of severe sepsis or signs of local infection, and replacement catheters were removed promptly if the previous catheter's tip was found to be colonized.

Definitions

As recommended by the Centers for Disease Control and Prevention,[5] catheter colonization was defined as growth of $\geq$15 colony-forming units from a distal catheter segment, and exit site infection was defined as erythema or induration within 2 cm of the catheter exit site in the absence of concomitant BSI and without concomitant purulence. The relationship between BSIs and CVCs was based on clinical and microbiological data, and classified as follows:

- probable – blood culture growing an organism commonly associated with catheter colonization in the absence of other sources of bacteraemia/fungaemia;
- definite – bacteraemia/fungaemia in a patient with an intravascular catheter with at least one positive blood culture obtained from a peripheral vein, clinical manifestations of infection and no apparent source for the BSI except the catheter, and at least one of the following: positive semi-quantitative cultures of peripheral blood and CVC tip yielding identical organisms (at species and antibiogram levels), or positivity for the same organism in blood cultures drawn simultaneously from the CVC and from a peripheral site, where the latter culture became positive >2 h after that drawn from the central line; or
- none (in the absence of the above findings).

Randomization and blinding

Patients were randomized to Group A [standard triple-lumen, non-medicated CVC; conventional catheter (CC)] or Group B