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A European perspective on intravascular catheter-related infections: report on the microbiology workload, aetiology and antimicrobial susceptibility (ESGNI-005 Study)

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ABSTRACT

The laboratory workload, microbiological techniques and aetiology of catheter-related infections in European hospitals are mostly unknown. The present study (ESGNI-005) comprised a 1-day (22 October 2001), laboratory-based, point-prevalence survey based on a questionnaire completed by microbiology laboratories in European (European Union (EU) and non-EU) hospitals. Also included were questions requesting retrospective information for the year 2000. In total, 151 hospitals from 26 European countries participated, of which 78.1% were teaching institutions. Overall, the estimated population served by these institutions was 121 363 800, and the estimated number of admissions during 2000 was 6 712 050. The total number of catheter tips processed during 2000 was 142 727, or 21/1000 admissions, of which 23.7% were considered to be positive in the institutions using semiquantitative or quantitative techniques. Overall, EU centres received significantly more catheter tip samples/1000 admissions and had a significantly higher rate of 'positivity' ($p < 0.0001$) than non-EU centres. Of the institutions surveyed, 11.4% (7.2% in EU countries and 23.7% in non-EU countries; p 0.04) used only qualitative techniques for catheter tip sample processing. On the day of the study, 167 microorganisms were recovered from significant catheter tip cultures (122 patients), of which Gram-positive bacteria represented 70.7%, Gram-negative bacteria 22.2%, and yeasts 7.2%. The five most common microorganisms were coagulase-negative staphylococci, *Staphylococcus aureus*, *Candida* spp., *Enterococcus* spp. and *Pseudomonas* spp. Overall, 19% of catheter tip cultures were polymicrobial. In the case of *S. aureus*, 40% of isolates were resistant to oxacillin, as were 63.4% of coagulase-negative staphylococcus isolates. Of 37 Gram-negative isolates, 35% were resistant to cefotaxime, 31% to ceftazidime, and 27% to ciprofloxacin. Imipenem and cefepime had the lowest reported rates of resistance (11%).

Keywords Catheter tip, epidemiology, intravascular catheter-related infections, laboratory workload, microbiology techniques, nosocomial infections

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INTRODUCTION

Intravenous catheter-related infections (IV-CRIs) are common nosocomial infections, which are currently responsible for >60% of nosocomial bacteraemic episodes in European hospitals [1]. Culture of catheter tips with semiquantitative or quantitative methods is currently the standard microbiological test for the diagnosis of catheter colonisation and is an essential part of the diagnosis of catheter-related bloodstream infections [2]. The techniques used to diagnose catheter colonisation in European microbiology laboratories have not been clearly defined and the corresponding workload is not known.

The aim of this study by the ESCMID Study Group on Nosocomial Infections (ESGNI) was to obtain general information on the microbiology

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workload and techniques used for IV-CRI diagnosis in Europe, as well as the aetiology and antimicrobial susceptibility patterns of pathogens causing intravenous catheter colonisation (IV-CC). The clinical aspects of intravascular catheter-related bloodstream infection will be considered separately.

MATERIALS AND METHODS

The present study (ESGNI-005) was a 1-day (22 October 2001), laboratory-based, point-prevalence study based on a questionnaire sent to the microbiology laboratories of every European hospital with one or more ESGNI members (*c.* 400 invitations to participate). The questionnaire also included a request for information on the results for the year 2000 in the participating laboratories.

The questionnaire requested information on the population served by the hospital, total number of beds, total number of admissions, total number of catheter tips sent to microbiology laboratories, and whether a qualitative, semiquantitative or quantitative technique was used for processing. Also requested was information on the total number of sterile samples and total number of significant positive samples (≥ 15 CFU/mL of any semiquantitative culture, or any quantitative culture yielding $\geq 10^3$ CFU) processed during the year 2000. Furthermore, information on the use of indirect methods of assessing catheter tip colonisation was requested (e.g., comparative quantitative blood cultures, skin and hub semiquantitative cultures, differential time to growth between blood cultures taken from peripheral veins and catheters).

For each episode of IV-CC on the day of study, information was requested regarding the microorganisms present and their antibiotic susceptibility profile, regardless of the laboratory method used for detection. The list of antimicrobial agents studied included: penicillin, ampicillin, ticarcillin, amoxycillin–clavulanate, oxacillin, cefazolin, cefuroxime, cefotaxime, ceftazidime, cefepime, imipenem, aztreonam, co-trimoxazole, ciprofloxacin, levofloxacin, gentamicin, tobramycin, amikacin, streptomycin, rifampicin, erythromycin, clindamycin, vancomycin, tetracycline and chloramphenicol.

Definitions

IV-CC was defined as any semiquantitative culture yielding ≥15 CFU, or any quantitative culture yielding $\geq 10^3$ CFU of bacteria or fungi. Any colony counts below these levels were considered to be negative. Data from institutions using qualitative techniques for catheter tip processing were not included in the study.

Data analysis

Discrete variables were expressed as percentages, and continuous variables as the mean and standard deviation when normally distributed, or as the median and interquartile range if their distribution was not normal. For discrete variables with missing values, percentages were calculated from the total of valid cases whenever missing values did not exceed 20% (in these instances, the variable was excluded from the analysis). Student's unpaired *t*-test was used to compare continuous variables, the Mann–Whitney *U*-test to compare continuous variables not normally distributed, and the chi-square or Fisher exact test to compare proportions. All statistical tests were two-tailed.

RESULTS

In total, 151 hospitals from 26 countries participated in the study (Table 1), comprising 111 hospitals from 12 European Union (EU) countries and 40 hospitals from 14 non-EU countries.

Laboratory workload of IV-CC during 2000

Of the 151 participating institutions, 78.1% and 21.9%, respectively, were teaching and non-teaching institutions. Hospital sizes varied from < 500 beds (34%), to 500–1000 beds (40.4%) and > 1000 beds (25.2%). Overall, the estimated population served by these institutions was 121 363 800, and the number of estimated admissions during 2000 was 6 712 050.

Results regarding the microbiology workload in 2000 are shown in Table 2. The total number of catheter tips processed during 2000 was 142 727, or 21/1000 admissions, of which 23.7% were considered to be positive in the institutions using semiquantitative or quantitative techniques.

Table 1. Distribution of participating hospitals (n = 151)

Country	No. of participating hospitals (%)	Country	No. of participating hospitals (%)
Austria	3 (2)	Malta	1 (0.7)
Belgium	10 (6.6)	The Netherlands	2 (1.3)
Bosnia-Herzegovina	2 (1.3)	Norway	1 (0.7)
Croatia	3 (2)	Poland	2 (1.3)
Czech Republic	5 (3.3)	Portugal	1 (0.7)
Denmark	1 (0.7)	Romania	1 (0.7)
France	11 (7.3)	Slovak Republic	4 (2.6)
Germany	12 (7.9)	Slovenia	2 (1.3)
Greece	14 (9.3)	Spain	32 (21.2)
Hungary	1 (0.7)	Sweden	1 (0.7)
Italy	17 (11.3)	Switzerland	3 (2)
Israel	1 (0.7)	Turkey	13 (8.6)
Lithuania	1 (0.7)	UK	7 (4.6)

Table 2. Microbiology workload associated with catheter tip samples in the year 2000

	EU countries (n = 111)	Non-EU countries (n = 40)	Total (n = 151)
Total catheter tip samples	108 243	34 484	142 727
Total no. of admissions	4 263 850	2 448 197	6 712 047
Catheter tip samples/1000 admissions year[a]	25	14	21
Positive samples (%)	28 502 (26.3%)[a]	5391 (15.6%)	33 893 (23.7%)

[a]$P < 0.0001$.

Overall, EU centres received significantly more catheter tip samples/1000 admissions, and had a significantly higher rate of 'positivity' ($p < 0.0001$) than non-EU centres.

Diagnostic techniques used in different institutions

Of all the institutions surveyed, 11.4% (7.2% in EU countries and 23.7% in non-EU countries; p 0.04) used only qualitative techniques to process catheter tip samples. Most (63.8%) institutions processed these samples using semiquantitative techniques, with no significant differences between EU and non-EU countries. Quantitative techniques were used in 24.8% of microbiology laboratories (27.9% in EU countries vs. 15.8% in non-EU countries; p 0.07) (Table 3). In 68.5% of the participating institutions, an indirect method of assessing catheter colonisation, e.g., comparative quantitative blood culture, infusate culture, internal brushing, and skin or hub culture, was used. These methods were used most frequently in EU countries (75.7% vs. 47.4%; p 0.02).

Microbiology results on the study day

Data regarding microbiology workload obtained on the day of the study differed only slightly from the questionnaire data relating to the year 2000. On the day of the study, 676 catheter tip samples were cultured in 151 institutions. Assuming a similar number of admissions in the year 2001, the estimated number of catheter tip samples during the day-prevalence study was 36.8/1000 admissions. According to the criteria of each individual laboratory, 168 (25%) samples were reported as positive (Table 4).

It was possible to collect information for 122 positive catheter tip samples, of which 94 were from EU countries and 28 from non-EU countries. These samples were taken from patients in intensive care units (41%), surgical services (25.4%) and general medical services (23.8%).

Table 3. Techniques used for the diagnosis of catheter tip infection

	EU countries (n = 111)	Non-EU countries (n = 40)	Total (n = 151)
Only qualitative techniques[a]	7.2%	23.7%	11.4%
Semiquantitative or quantitative techniques	9.9%	10.5%	10%
Only semiquantitative techniques	64.9%	60.5%	63.8%
Only quantitative techniques	18%	5.3%	14.8%

[a]p 0.04.

Table 4. Data for catheter tip samples obtained on the study day (22 October 2001)

	EU countries (n = 111)	Non-EU countries (n = 40)	Total (n = 151)
Total catheter tip samples	506	170	676
Total positive samples	132 (26%)	36 (21%)	168 (25%)

The number of microorganisms isolated on the day of the study from significant catheter tip cultures was 168 (Table 5). Overall, 19% of cultures were polymicrobial. Gram-positive bacteria comprised 70.7% of all isolates, and Gram-negative bacteria 22.2%. Yeasts were isolated from 7.2% of catheter tip samples. The five organisms isolated most commonly were, in decreasing order: coagulase-negative staphylococci, *Staphylococcus aureus*, *Candida* spp., *Enterococcus* spp. and *Pseudomonas* spp. The organisms isolated were similar in both groups of hospitals (EU and non-EU), with the single exception of *S. aureus*, which was isolated more frequently in non-EU countries (34.3% vs. 6.1%; $p < 0.0001$). While *Candida* was the second most frequently isolated microorganism in catheter tips in EU countries (9.1%), laboratories from non-EU countries did not report any *Candida* isolates; however, this difference did not reach statistical significance (p 0.2).

Resistance patterns of the most frequent isolates

Table 6 lists the antibiotic resistance data for organisms isolated from catheter tips in the different centres. The sensitivity assays were not performed in a central laboratory, and local susceptibility testing results were taken at face value. In the case of *S. aureus*, 40% of isolates were resistant to oxacillin, as were 63.4% of coagulase-negative staphylococcus isolates. Of the 118 Gram-positive isolates from catheter tips in Europe, 51.5% were oxacillin-resistant, but vancomycin was reported to be active against all but two single isolates (coagulase-negative staphylococcus and *E. faecalis*). Of the 37 Gram-negative organisms isolated, only 65% were susceptible to cefotaxime, and only 69% to ceftazidime. Ciprofloxacin resistance was reported for 27% of these isolates, with imipenem and cefepime having the lowest reported rates of resistance (11%). Imipenem-resistant Gram-negative organisms

Table 5. Organisms isolated from catheter tip samples

EU countries (n = 132)		Non-EU countries (n = 36)		Total (n = 168)	
Organism	**No. (%)**	**Organism**	**No. (%)**	**Organism**	**No. (%)**
CONS	68 (51.5%)	CONS	14 (40%)	CONS	82 (49.1%)
Candida spp.[a]	12 (9.1)	*S. aureus*[b]	12 (34.3)	*S. aureus*	20 (11.9)
S. aureus[b]	8 (6.1)	*Acinetobacter* spp.	2 (5.7)	*Candida* spp.	12 (7.2)
Pseudomonas spp.	7 (5.3)	*Corynebacterium* spp.	2 (5.7)	*Enterococcus* spp.	9 (5.9)
Enterobacter spp.	6 (4.5)	*Enterococcus* spp.	2 (5.7)	*Pseudomonas* spp.	8 (4.9)
Enterococcus spp.	6 (4.5)	*Enterobacter* spp.	1 (2.9)	*Acinetobacter* spp.	7 (4.2)
Acinetobacter spp.	5 (3.8)	*Klebsiella* spp.	1 (2.9)	*Enterobacter* spp.	7 (4.2)
Klebsiella spp.	5 (3.8)	*Pseudomonas* spp.	1 (2.9)	*Klebsiella* spp.	6 (3.6)
Proteus spp.	4 (3)	Others	1 (2.9)	*Proteus* spp.	4 (2.4)
E. coli	3 (2.3)			*Corynebacterium* spp.	4 (2.4)
Corynebacterium spp.	2 (1.5)			*E. coli*	3 (1.8)
Others	6 (4.5)			Others	6 (3.6)

CONS, coagulase-negative staphylococci.
[a]Speciation of *Candida* isolates was not requested in the questionnaire.
[b]$p < 0.0001$.

Table 6. Overall resistance rates in organisms isolated from catheter tip cultures

Antimicrobial agents tested	Gram-negative bacteria	Gram-positive bacteria	*S. aureus*	CONS
Cefotaxime	13/37 (35%)	NT	NT	NT
Ceftazidime	12/37 (31%)	NT	NT	NT
Cefepime	4/37 (10.8%)	NT	NT	NT
Imipenem	4/37 (10.8%)	NT	NT	NT
Ciprofloxacin	10/37 (27%)	NT	NT	NT
Oxacillin	NT	61/118 (51.5%)	8/20 (40%)	52/82 (63.4%)
Vancomycin	NT	2/118 (1.7%)	0	1/82 (1.2%)

CONS, coagulase-negative staphylococci; NT, not tested.

comprised three *Acinetobacter* isolates and one *Pseudomonas* isolate.

DISCUSSION

Most literature on clinical microbiology, infectious diseases and laboratory medicine gives no insight into the workload generated by catheter tip sampling in microbiology laboratories. The present data, obtained from 151 hospitals in Europe, show that 21 catheter tip cultures were processed/1000 admissions in 2000, with a significant difference between the workloads in EU and non-EU hospitals. EU hospitals processed more samples each year, with a higher rate of positivity, which could partly reflect more invasive procedures in EU countries, with a parallel higher use of central intravenous lines. It should be noted that new guidelines discourage routine culturing of all removed catheters, and only recommend culturing catheters from patients when bloodstream infection is suspected.

Although qualitative culture has no role in the diagnosis of IV-CC [3–5], and should be clearly discouraged, it was the only method used in >11% of European laboratories, most of which were in non-EU countries. Fortunately, most laboratories use the recommended techniques, and in >23% of EU microbiology laboratories, the most recent quantitative methods have replaced Maki's semiquantitative catheter tip culture.

In parallel, more conservative diagnostic tests, which do not depend on catheter withdrawal, have been developed. These include comparative quantitative blood cultures taken from a catheter and peripheral veins [6], skin and hub cultures [7], and differential time of growth between blood obtained from a catheter and that obtained from peripheral veins [8]. The wide use of these techniques reported in the present study (nearly 70%) seems to be proof of the acceptance in European institutions of conservative diagnostic techniques for IV-CRI. Nevertheless, it should not be inferred that these institutions are using such techniques exclusively on a day-to-day basis.

The aetiology of IV-CRI in Europe, as shown in the present study, is associated mostly with Gram-positive microorganisms (coagulase-negative staphylococci and *S. aureus*), as reported in other European studies [9, 10]. *Candida* spp. is the third most common pathogen isolated in cases of IV-CRI, reflecting the reported rising trend of this microorganism as a major nosocomial pathogen in developed countries [11–13]. The significance of the higher incidence of *S. aureus* in non-EU countries cannot be explained clearly, although it may be associated with differences in the procedures employed in the insertion of intravascular catheters and in operating theatres, as well as antiseptic measures, etc.

The resistance patterns of the IV-CRI isolates reported in this study should be considered with caution for several reasons: the study was not

designed to evaluate the resistance rates directly, the isolates were not tested in a central laboratory, and only a few microorganisms were studied. However, some interesting inferences were drawn from the data in this study. There were high rates of resistance in Gram-negative isolates from catheter tips (> 30% to cefotaxime and ceftazidime, and nearly 30% to ciprofloxacin). A similar observation was made in a European study of nosocomial bacteraemia isolates by Dornbusch *et al.* [14], in which it was also noted that countries previously belonging to the 'eastern block' had higher rates of resistance. Another concern was that 40% of *S. aureus* isolates from catheter tips were oxacillin-resistant in the present study, which supports the use of glycopeptides as first-line empirical antimicrobial agents for catheter-related bloodstream infections.

In conclusion, the microbiological diagnosis of IV-CRI is increasingly more effective in European institutions, but there are still some deficiencies in the techniques used, especially in non-EU countries. The recognition of new pathogens such as *Candida* spp., and the increasing rates of antibiotic resistance in Gram-positive and Gram-negative bacteria, stress the need for a general European surveillance system.

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