SPIR01 and SPIR02: a two-year 1-day point prevalence multicenter study of infections in intensive care units in Piedmont, Italy

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SUMMARY

This study reports the results of a one-day point prevalence study of infections performed in 2001 (SPIR01) and 2002 (SPIR02) in a Regional network of ICUs in Piedmont, Italy. The study aims were to illustrate the overall proportion of infected patients and the rate of ICU-acquired infections. Mortality rate was evaluated three weeks after the study days. Resistance pattern of *Staphylococcus aureus*, coagulase negative Staphylococci and *Pseudomonas aeruginosa* were recorded. The primary end-point of the study was to document the prevalence and associated risk factors of the ICU-acquired infections, and the impact of infections on mortality. The prevalence of ICU-acquired infection was 30% in SPIR01, and 38.3% in SPIR02. The rate of methicillin-resistance was high among isolates of *Staphylococcus aureus* and coagulase-negative Staphylococci. The prevalence of ICU-acquired infections was lower than that reported in the EPIC study. In our experience, this Regional survey stimulated further research and collaboration to improve the prophylaxis, diagnosis and treatment of ICU-acquired infections.

KEY WORDS: Nosocomial infections, Prevalence, Intensive care units

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INTRODUCTION

Nosocomial infections are associated with increased morbidity and mortality and may affect as many as 30% of patients admitted to the Intensive Care Unit (ICU) (Vincent 2003). Factors associated with ICU-acquired infections may be related to diagnostic or therapeutic indwelling devices such as central venous and urinary catheters, sedation, administration of steroids or immunosuppressive treatment, wound and drainage, but also include cross-transmission of microrganisms from the health-care personnel, body position and a variety of specific and unspecific alteration of the host response (Vincent *et al.*, 1995).

Nosocomial infections include respiratory tract infections and ventilator-associated pneumonia (VAP), central venous catheter bloodstream infections (CVC-BSI), urinary tract and wound infections which are often caused by multi-drug re-

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sistant (MDR) bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum beta-lactamase (ESBL) producing Gram-negative bacilli (*Klebsiella pneumoniae*, *Escherichia coli*) and MDR *Pseudomonas aeruginosa* (Vincent 2003).

According to the Study on the Efficacy of Nosocomial Infection Control (SENIC), one third of nosocomial infections may be avoided with appropriate programs of infection surveillance and control (Haley RW *et al.,* 1985). The EPIC study was a European multicenter 1-day point-prevalence study of 1417 ICUs which examined 10,038 patient case reports, and provided data on rates of ICU-acquired infections, antimicrobial consumption, pattern of resistance of isolated bacteria, and potential risk factors for ICU-acquired infections and death (Vincent *et al.,* 1995). The EPIC study was the first large European database which served as a reference for improvement in preventing nosocomial infections.

In this brief report we describe the results of an Italian regional multicentric 1-day point-prevalence study performed in 2001 (SPIR01) and 2002 (SPIR02), the primary aim of which was to determine the prevalence and the risk factors of ICU-acquired infections, and to identify the predominant infecting microrganisms. Furthermore, the relationship between ICU-acquired infections and mortality was established recording each patient outcome (death or survival) at 3 weeks of follow-up.

MATERIALS AND METHODS

A 1-day point-prevalence study was performed on June 27, 2001 (SPIR01) and July 10, 2002 (SPIR02) in the ICUs of the North-Western Region of Italy, namely Piedmont and Valle d'Aosta. Eighteen out of the 33 (54.5%) mixed (medical and surgical) ICUs in Piedmont and Valle d'Aosta participated in SPIR01, and 20 out of 33 (60.6%) participated in SPIR02, including a Neurosurgical and a Cardiosurgical ICU. Coronary care units, specialized paediatric units and special care infant units were excluded from the survey.

The study population was defined as all patients occupying a bed over the 24-hour study-periods. Patients aged less than 12 years were excluded.

For each patient the following data were reported: demographics, category of patient (medical, post-surgery, post-trauma), underlying diseases, clinical status on admission evaluated with Simplified Acute Physiologic Score (SAPS) II score, predisposing factors and diagnosis of admission in ICU. Diagnostic and therapeutic interventions, including antibiotic treatment, were detailed and reported up to one week before the study days.

Recorded risk factors for ICU-acquired infections were urinary catheters and CVC, arterial or pulmonary artery catheter, mechanical ventilation, total parenteral nutrition, indwelling pleural or surgical drainage, tracheostomy, haemodialysis or continuous haemofiltration, presence of invasive devices to monitor intracranial pressure, peritoneal dialysis, sedation for more than 6 hours, high dose or >10 days duration of corticosteroid therapy, other immunosuppressive treatment, stress gastrointestinal ulcer prophylaxis and type (use of anti-H2 antagonists or sucralfate or pump-inhibitor, other anti-acid medications), selective decontamination of the digestive tract.

The presence or absence of infection by type was assessed using the standard definitions of the Centers for Disease Control and Prevention (CDC) (Garner JS *et al.,* 1988). Each reported infection was classified either as community-acquired (infections occurring in the community and manifesting at the time of hospital admission), hospital-acquired (manifest at the time of ICU admission and interpreted as related to the hospital admission), or ICU-acquired (diagnosed in the ICU, active or under treatment at the time of the study, but not clinically manifest at the time of the ICU admission).

Microbiological data were recorded and included bacteriologic studies requested on the day of the study or before and available within 1 week after the study day. Isolates from the bloodstream, the respiratory and urinary tract were considered significant.

Patient outcome (death or survival) was assessed 3 weeks after the study days. Study forms were filled by a Medical Doctor in each ICU and faxed centrally to the coordinating centre (Department of Infectious Diseases, Turin). Statistical analysis was performed with Statview 5.0 (Abacus Concept).

RESULTS

Prevalence of infections and associated risk factors

In SPIR01 data from 197 patients (M=131, F=66, mean age 60.15 (range 13-94 years) were analysed, and 91 (46.2%) were infected on the study day, with some patients having more than one infection. The prevalence rates of community-, hospital-, and ICU-acquired infections were 9% (18/197), 15.7% (31/197), and 22% (43/197), respectively. Among the 91 infections there were 43 pneumonias (47.2%), 20 UTIs (18.5%) and 11 (12%) laboratory-confirmed bloodstream infections.

In SPIR02 data from 201 patients (M = 128 and F =73, mean age 61.73 (range 17-90 years) were analysed, and 98 (48.7%) had at least one infection on the study day. The prevalence rates of community-, hospital- and ICU-acquired infection were 14.4% (29/201), 12.4% (25/201) and 28% (56/201), respectively. Among the 98 infections there were 40 (41%) pneumonias, 20 (20.4%) UTIs and 18 (18.3%) laboratory-confirmed blood stream infections.

The prevalence and risk factors for the ICU-acquired infections in SPIR01 and SPIR02 are given in Tables 1 and 2, respectively.

In SPIR01, both an ICU-acquired infection ($p<0.0001$, 95% C.I. 11-28.4), and pneumonia ($p=0.03$) were significantly associated with longer duration of ICU stay. Higher SAPS II scores at admission were also significantly associated with an ICU-acquired infection ($p=0.032$; mean difference 8.4, 95% C.I. 2.8-13.9) and with mortality ($p=0.0005$; mean difference 9.4; OR 4.2-14.6).

In SPIR02, an ICU-acquired infection was significantly associated with longer duration of ICU stay ($p=0.0022$, 95% C.I. 5.4-24.2). The mean SAPS II score at admission was not significantly different in patients who developed an ICU-acquired infection or those with adverse outcome.

Microbiology

The microganisms isolated in patients with ICU-acquired infections were the following.

In SPIR 01 three coagulase-negative staphylococci were isolated (two of these were methicillin-resistant), and 10 isolates of *S. aureus* (8 methicillin-resistant). *P. aeruginosa* was isolated in 12 cases, and six strains were resistant to one or more of the following antibiotics: gentamycin sulphate (4), imipenem (3), ceftazidime (3), ciprofloxacin (3) and piperacillin/tazobactam (5). There was an *Enterococcus faecalis* strain which was susceptible to vancomycin.

TABLE 1 - *Frequencies of ICU-acquired infections.*

ICU-acquired Infection Type	*SPIR01 No. (%)*	*SPIR02 No. (%)*
Pneumonia	19 (44.2)	18 (32.1)
Lower respiratory tract (not pneumonia)	17 (39.5)	18 (32.1)
Urinary tract	10 (23.3)	13 (23.2)
Laboratory-confirmed bloodstream	7 (16.3)	14 (25.0)
Surgical wound	0 (0.0)	2 (3.6)
Ear, nose and throat	2 (4.6)	1 (1.8)
Skin and soft tissue	1 (2.3)	1 (1.8)
Gastrointestinal	0 (0.0)	3 (5.3)
Cardiovascular	0 (0.0)	1 (1.8)
Clinical sepsis	5 (11.6)	9 (16.1)
Central nervous system	0 (0.0)	0 (0.0)

TABLE 2 - *Risk factors for ICU-acquired infections in SPIR01 and SPIR02.*

Risk factors	*SPIR01 No. (%)*	*SPIR02 No. (%)*
Urinary catheter	188 (95.4)	191 (95.0)
Central intravenous catheter	173 (87.8)	177 (88.0)
Mechanical ventilation	164 (83.2)	160 (79.6)
Arterial catheter	126 (64.0)	147 (73.1)
Central intravenous nutrition	68 (34.5)	68 (33.8)
Chest or wound drain	42 (21.3)	45 (22.4)
Pulmonary artery catheter	8 (4.0)	6 (3.0)
Tracheostomy	77 (39.1)	60 (29.8)
Haemodialysis	15 (7.6)	12 (6.0)
Intracranial pressure monitoring	7 (3.5)	17 (8.4)
Peritoneal dialysis	0 (0.0)	0 (0)
Sedation	98 (49.7)	104 (51.7)
Long-term/high-dose steroids	8 (4.0)	8 (4.0)
Immunosuppressant therapy	3 (1.5)	5 (2.5)
Stress ulcer prophylaxis*	159 (80.7)	169 (84.1)
H2 receptor antagonist	85 (43.1)	81 (40.3)
Sucralfate	36 (18.3)	30 (15.0)
Antacids	3 (1.5)	2 (1.0)
Omeprazole	51 (25.9)	78 (38.8)
Selective digestive decontamination	9 (4.6)	3 (1.5)
Prophylactic antibiotics	41 (20.8)	45 (22.4)

*Some patients received more than one regimen for stress ulcer prophylaxis.

In SPIR 02 there were 10 coagulase-negative staphylococci isolated (nine of these were methicillin-resistant), and 31 isolates of *S. aureus* (17 methicillin resistant). *P. aeruginosa* was isolated in 28 cases, and 20 strains were resistant to one or more of the following antibiotics: gentamycin sulphate (15), imipenem (9), ceftazidime (11), ciprofloxacin (12), or an ureido-penicillin (12). There were five isolates of *E. faecalis/faecium*, of which only one was vancomycin-resistant.
All the reported isolates were found in bloodstream or respiratory tract samples with a compatible clinical picture.

In SPIR01 at the time of the study days the majority of patients were receiving antibiotic treatment and only 16.7% of patients were not treated with antibiotics. Antibiotics were administered for prophylaxis in 38 (19.3%) cases. The most widely used were beta-lactams (72.6%), with only five patients (2.5%) receiving double beta-lactams treatment for a diagnosis of Gram-negative infections.
In SPIR02 at the time of the study days the majority of patients were receiving antibiotic treatment and only 14.5% of patients were not treated with antibiotics. Antibiotics were administered

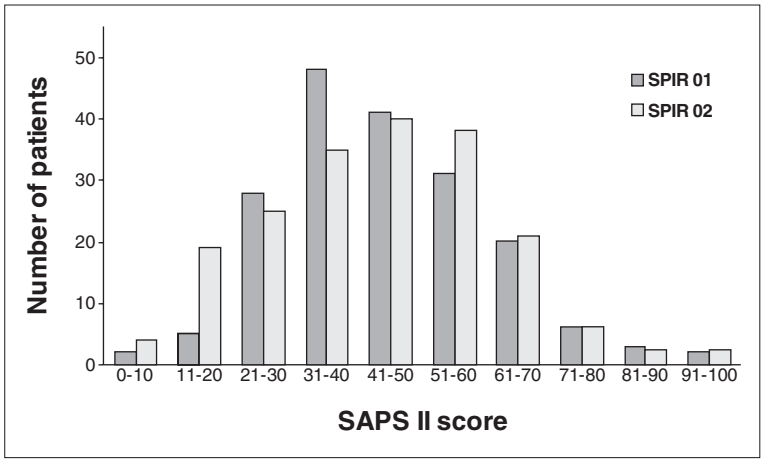

FIGURE 1 - *SAPS II score at admission for SPIR 01 (N=186) and SPIR 02 (N=192).*

for prophylaxis in 41 cases (20.6%). The most widely used were beta-lactams (69.7%), with 14 patients (7%) receiving double beta-lactams treatment for prophylaxis in five cases and treatment in nine cases.

The mean SAPS II Score at ICU admission was 45.2±16.2 and 43±18.1 in SPIR01 and SPIR02, respectively (Figure 1).

The overall mortality at three weeks was 26% (49 out of 188) and 25% (50 out of 198) in SPIR01 and SPIR02, respectively. The mortality at three weeks was significantly associated with the SAPS II Score at admission only in SPIR01 (p=0.0005 for unpaired comparison, mean difference 9.4, 95% C.I: 4.2-14.6). There was no statistically significant association with mortality and any of the parameters studied in SPIR02.

DISCUSSION

This study was performed to explore the regional prevalence of infections in ICUs and to compare it with European data available from the EPIC study, which reported that among the 14 Countries participating Italy ranked 5th as number of participating ICUs, 7th among number of patients contributing to the study, 2nd for the prevalence of community- hospital-acquired infections and 14th for the prevalence of ICU-acquired infections, with the 6-week mortality rate ranking 12th (Vincent JL, Bihari D *et al.,* 1995). The prevalence rates of ICU-acquired infections were 21.8% and 27.9%, respectively in SPIR01 and 48.7% in SPIR02.

Overall, the infection rates in our study were similar to those reported in the EPIC study and were lower than those recorded in the Italian participating ICUs [Vincent JL *et al.,* 1995; Orsi GB *et al.,* 2003; Luzzati R *et al.,* 2001.]. The main differences between SPIR01-02 and the EPIC study are highlighted in Table 3. In our study there was a higher rate of community and hospital-acquired infections and a slightly higher mortality rate, but there was a lower rate of ICU-acquired infections (Table 2). We agree that it may be difficult to com-

TABLE 3 - *Comparison with the Italian data contributing to the EPIC study.*

	No. of ICUs	*No. of Patients*	*Prevalence of Infection (%)*			*ICU Mortality Rate (%)**
			Community	*Hospital*	*ICU*	
Italian ICUs in the EPIC study	110	617	8.8	7.8	31.6	20.3
SPIR01	18	197	9.1	15.7	21.8	24.8
SPIR02	20	201	14.4	12.4	27.9	24.9

*Mortality at siz weeks in the EPIC study and at three weeks in SPIR01 and SPIR02.

pare these infection rates without considering the type of the ICU, the percentage of patients admitted after major trauma or surgery and the duration of ICU stay. For example, the higher number of ICU infections in SPIR02 were possibly related to the presence of Cardiosurgical and Neurosurgical ICUs. However, we believe that it is important to pay ongoing attention to the epidemiology of ICU-acquired infections and to explore the epidemiology at a multicenter level to provide the best care and to stimulate collaboration among different Hospitals.

The mortality rate was evaluated at three weeks in our study compared with the six weeks in the EPIC study. The higher mortality rate in SPIR01 was significantly associated with the SAPS II score at admission suggesting that, at least in SPIR 01, there was a large proportion of patients admitted to the ICU with a poor prognosis.

The main isolates were Gram-negative bacilli (*E. coli, Klebsiella spp*. and *P. aeruginosa*) and Gram-positive cocci, mainly *S. aureus* and *S. epidermidis*. Among patients with ICU-acquired infection caused by *S. aureus*, the methicillin-resistance rate was 80% and 55%, respectively in SPIR01 and SPIR02. The rate of methicillin-resistance was higher in SPIR01 (80%) than in SPIR02 (55%). In the EPIC study it was 72.4% and it was similar to a study performed in Veneto, northeast of Italy, (75%) (Vincent *et al.,* 1995; Luzzati *et al.,* 2001). Amongst the isolates of *P. aeruginosa* there was a high resistance rate which couples with the high exposure to antibiotics in the ICU setting, as demonstrated by the fact that only a minority of patients included in our study did not receive any antibiotic treatment. Compared to EPIC study, the percent of resistance of *P. aeruginosa* was higher for ceftazidime (42.8% Vs. 27.7%) and fluoroquinolones (46.4% Vs. 26.3%), and identical for aminoglycosides (46%) (Vincent *et al.,* 1995).

Effective strategies to limit antibiotic resistance include increased diagnostic specificity, reduced antibiotic consumption and tailored antimicrobial treatment. Epidemiologic data are extremely important for the selection of the initial empiric antibiotic regimen, which has to be adapted to the local pattern of antibiotic resistance. As an alternative, antibiotic cycling may be a useful tool to reduce the rate of resistance of Gram-negative bacteria and restore a pattern of sensitivity (Raymond *et al.,* 2001; Kollef *et al.,* 1997; Gruson *et al.,* 2000; Gruson *et al.,* 2003.

Programs of active surveillance of nosocomial infections play an important role in detailing the local epidemiology and the local pattern of antibiotic resistance and they are critical for the development of effective preventive strategies. SPIR01 and SPIR02 are useful as a reference for future regional epidemiological studies, to discuss and implement interventions aimed at decreasing the rate of ICU-acquired infections. In our experience, the regional study is the simplest way to start a partnership with other colleagues who share the same problems.

One of the limitations of these studies is that they rely on diagnosis made by the referring centres, which have a different threshold for clinical diagnosis and which have different programs for infection control and hospital infection prophylaxis. For example, in the EPIC study there was a geographic difference and there was a north/south gradient, with higher rates of hospital acquired infections and higher mortality rates in Southern Europe (Vincent *et al.,* 1995). Collecting data at a regional level, in our opinion, is the starting point of comparison even at the diagnostic level and stimulate the institution of working groups. In Piedmont we are currently working with a regional network to improve the outcome of patients with sepsis and to improve the prophylaxis of ventilator-associated pneumonia in mechanically ventilated patients. SPIR01 and SPIR02 represent the basis for the implementation of prophylaxis, diagnosis and treatment of ICU-acquired infections.

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