MAJOR ARTICLE

Bloodstream Infections: A Trial of the Impact of Different Methods of Reporting Positive Blood Culture Results

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(See the editorial commentary by Cunha on pages 1170–3)

Background. The impact of how positive blood culture results are reported on the evolution bloodstream infections (BSIs) has not been assessed.

Methods. We randomly assigned patients with BSIs into 3 groups: group A (for which physicians received a conventional report), group B (for which physicians received a conventional report and a written alert on the chart with clinical advice), and group C (for which physicians received the above plus oral clinical advice). The adequacy of therapy before and after receipt of the different types of information was assessed.

Results. Overall, 297 episodes (109 in group A, 99 in group B, and 89 in group C) were studied. Patients who received inadequate treatment before receiving microbiological information had a longer mean ($\pm$ SD) hospital stay (27.2 $\pm$ 32.4 vs. 19.4 $\pm$ 15.8 days; $P = .017$), a higher mean risk of *Clostridium difficile*–associated diarrhea (8.3% vs. 1.9%; $P = .013$), a higher mean overall mortality rate (30.8% vs. 19.4%; $P = .025$), and a higher mean risk of infection-related mortality (23.3% vs. 13.6%; $P = .031$). After receipt of microbiological reports, recommendations for changes in therapy were issued for patients in groups B (52.3%) and C (53.1%). For groups A, B, and C, the proportions of days on which adequate treatment was received were 66.3%, 92.1%, and 91.2% ($P < .001$); the mean numbers of defined daily doses of appropriate antibiotic therapy were 16.4, 22.2, and 20.7 ($P = .003$); the mean durations of hospital stay were 19.8, 23.6, and 24.1 days ($P = .761$); and the mortality rates during the late period were 12.9%, 15.6%, and 11% ($P = .670$), respectively. The mean costs of antimicrobials per episode in groups A, B, and C were €580.63, €537.98, and €434.53 (US$707.85, US$699.73, and US$529.73, respectively).

Conclusions. Written- or oral-alert reports with clinical advice should complement traditional microbiological reports for patients with BSIs.

Several studies show that up to 40% of all patients with bloodstream infections (BSIs), 50% of those with nosocomially-acquired BSIs, and up to 70% of those with fungemia receive inadequate therapy during the empirical period (before microbiological information is available) [1–11]. Several articles have demonstrated that, even after the final microbiological report is issued, 8%–20% of patients with BSIs still receive inadequate antimicrobial treatment [4, 5, 8, 10, 11].

The documentation of BSIs in clinical records and the professional opinion of an infectious diseases specialist in the selection of antimicrobial agents may have an impact on the quality of clinical care [5, 12–14]. Our study reports the consequences of inadequate antimicrobial therapy and compared 3 different methods of reporting microbiological information and infectious diseases advice for patients with BSIs.

PATIENTS AND METHODS

Our institution is a general, teaching, and referral hospital with 1750 available beds covering an urban population of 650,000 persons.

Study Period and Patient Selection

The study was performed during the period of 1 February 2000 through 31 July 2000. We randomly selected

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data on 1 of every 2 episodes of significant BSI to be included in the study.

In cases involving microorganisms of doubtful significance (e.g., *Bacillus* species, nonhemolytic *Streptococcus* species, *Propionibacterium acnes, Corynebacterium* species, *Clostridium* species, and coagulase-negative *Staphylococcus* species), clinically relevant episodes were only episodes in which there was evidence of clinical manifestations of infection and no other explanation and in which the microorganisms were isolated in ⩾2 different blood cultures. In the few cases involving recurrent bacteremia, we only included the first episode in the study.

Processing of Samples in the Microbiology Laboratory

For blood cultures, we used an automated system (Bactec 9240; Becton Dickinson Microbiology Systems), with continuous agitation. Microorganisms were identified using standard procedures, and antimicrobial susceptibility tests were performed by broth microdilution using NCCLS breakpoints. Our study is a prospective, randomized comparison of 3 different models of interaction for reporting positive results of blood cultures.

Combined Microbiological and Clinical Report

We randomly classified the patients with significant episodes of bacteremia into 3 different groups by means of a computer-assisted random list.

Group A (i.e., conventional information provided). Immediately after the automatic detection of microbial growth, the physicians in charge are informed by telephone of the result of the Gram stain, and a written report is produced only after definitive identification and antimicrobial susceptibilities of the isolates are obtained.

Group B (i.e., written-alert report on the clinical chart). In this group of patients, the procedure for group A is complemented with a written-alert report issued at the bedside to be included with the clinical chart. The report includes a brief opinion on patient's situation based on the clinical records, including therapeutic recommendations.

Group C (i.e., oral-alert report provided). This procedure includes all the information provided to groups A and B together, as well as a direct conversation with the physician in charge.

Our institutional ethics review committee approved this investigation.

Clinical Data

The patient records for all 3 groups were reviewed after discharge from the hospital or death, without further intervention. The following clinical data were recorded: age, sex, hospital service, underlying diseases, comorbidities, severity of the clinical situation (APACHE II score), predisposing factors for bacteremia, clinical significance of blood culture results, place of acquisition of the BSI episode, and presence of septic metastasis. The duration, type, dose, and route of antibiotic therapy were recorded.

Definitions

Underlying diseases and comorbidities. For classification of underlying diseases, we used the McCabe and Jackson scale [15]. Comorbidities were assessed by use of the Charlson comorbidity score [16].

Predisposing factors. The following factors were considered: presence of indwelling catheters, presence of permanent prosthetic material, neutropenia, malnutrition, history of injection drug abuse, splenectomy, invasive procedures, corticosteroid therapy (equivalent to ⩾10 mg of prednisone per day for ⩾2 weeks or ⩾30 mg of prednisone per day for ⩾1 week), and antimicrobial therapy in the week before the BSI episode.

Origin and source of BSI. BSI was considered to have been community acquired if the first specimen to yield a positive blood culture result was obtained within the first 48 h of admission. After this delay (or before, if it was clearly related to an invasive procedure performed in the hospital), the infection was considered to be nosocomial. The source of BSI was documented if there were focal signs or symptoms of infection and/or the same microorganism was isolated from specimens of blood and from the infected site. In the absence of a recognized source, BSI was classified as primary.

Sepsis and death. Sepsis and septic shock were defined as proposed by Bone et al. [17]. Death was considered to be attributable to BSI if it occurred during the active infection phase or while the patient was undergoing antimicrobial treatment.

Antibiotic therapy. Antibiotic therapy was assessed during the following 3 periods.

1. The empirical period, which began at the time that the first blood culture sample was obtained and ended 24 h later.
2. The "early" period, which began when the first blood culture sample was obtained and ended when the final microbiological report was received. During this period, which includes the empirical period, the phone alert was issued and the Gram stain findings and the preliminary antibiogram became available.
3. The "late" period, which began when the definitive susceptibility test results were available and ended with death or when antimicrobial therapy for the episode was completed.

Data on antimicrobial therapy were obtained on a daily basis. Antimicrobials used to treat infections not related to the BSI episode were not considered. The total number of daily defined doses (DDD) and the number of appropriate DDDs used per BSI episode were also evaluated. Only changes in the thera-

peutic regimen made within 48 h of the final microbiological report were considered to be a consequence of these results.

Criteria for adequacy of therapy. Appropriate empirical therapy was defined as the administration of agents that were active in vitro against the infecting microorganism during the empirical period (i.e., the first 24 h of treatment) Adequate antimicrobial therapy was defined as that which fulfilled the criteria of proper indication, coverage, spectrum, dose, interval, route, and duration. These parameters were defined as follows.

1. Indication: the indication for antibiotic use was considered to be adequate if antibiotic therapy was indicated by the severity of the episode, and antibiotics were not to be used if blood cultures indicated contamination or if surgery or catheter extraction were enough to control the infection.
2. Coverage: coverage was regarded as adequate if the antibiotics administered were of clinically proven efficacy and active in vitro against the infecting microorganisms.
3. Spectrum: it was considered to be appropriate to use antimicrobials with a narrower spectrum if indicated by antimicrobial susceptibilities. This parameter was considered only after a bacterial pathogen was identified.
4. Dose: the dose was the universally accepted, literature-based dose for the antimicrobial used [18].
5. Interval: it was determined to be adequate to use the antimicrobials at the correct intervals according to pharmacokinetic data or serum levels.
6. Route: the route was considered to be appropriate if $\geqslant$3 days of intravenous treatment was administered for gram-negative bacteremia and if 10 days of intravenous treatment was administered for *Staphylococcus aureus* bacteremia, as per Byl el al. [14]. Switching to oral administration was considered to be appropriate if the infection was treatable using oral therapy, if a clinical response occurred during intravenous treatment, if digestive absorption was normal, and if drugs that would be adequately absorbed orally and active against the infecting microorganisms were available.
7. Duration: the duration was considered to be appropriate if there was completion of 10–14 days of therapy for non-complicated BSI and of >2 weeks of therapy in the presence of endocarditis, osteomyelitis, or permanent prosthetic material.

Statistical Analysis

Relationships between variables were evaluated using the χ^2 statistic for categorical variables, Student's t test for normally distributed continuous variables, and the Mann-Whitney U test for nonparametric comparisons. Univariate correlates and clinically significant variables ($P < .05$) were then entered into stepwise logistic regression analyses. Factors with $P < .05$ were retained in the model. The statistical analysis was performed using SPSS software, version 10.0 (SPSS).

RESULTS

During the study period, 12,643 blood samples were processed at our microbiology laboratory. Overall, 581 clinical episodes of significant bacteremia/fungemia were detected. After random selection, 297 episodes were included in the study and were randomly assigned to 1 of 3 information groups, as follows: group A (those who received conventional information), 109 episodes; group B (those who received conventional information and a written-alert report), 99 episodes; and group C (those who received conventional information and both written- and oral-alert reports), 89 episodes.

Patient Characteristics

The demographic and clinical characteristics of patients with BSI and the microorganisms isolated are summarized in table 1, which compares the 3 groups in the study. The univariate analysis did not show any differences among the 3 groups.

Adequacy of Empirical Antimicrobial Therapy

During the empirical period, 58.5% of patients received appropriate antimicrobial therapy. Adequacy was similar for groups A, B, and C (57%, 61.1%, and 57.5%, respectively; $P = .823$). Inappropriate treatment was prescribed to 27.7% of subjects, whereas 13.7% of subjects received no antimicrobial treatment.

Univariate analysis revealed that the risk factors for inadequate antimicrobial therapy included the presence of fungemia, nosocomial infection, and previous receipt of antimicrobial therapy. BSI caused by *Escherichia coli* and *Streptococcus pneumoniae* and the presence of septic shock were associated with a lower risk of inadequate treatment (table 2).

Compared with patients who received adequate treatment, patients who received inadequate treatment during the empirical period had a longer hospital stay (mean $\pm$ SD, 27.2 $\pm$ 32.4 vs. 19.4 $\pm$ 15.8 days; $P = .017$), a higher risk of nosocomial *Clostridium difficile*–associated diarrhea (8.3% vs. 1.9%; $P = .013$), a higher overall mortality rate (30.8% vs. 19.4%; $P = .025$), and a higher risk of infection-related mortality (23.3% vs. 13.6%; $P = .031$) (table 3). Multivariate analysis revealed that inappropriate treatment was an independent risk factor for increased mortality, as shown in "Factors that Predict Increased Mortality on Multivariate Analysis," below.

Evaluation of the 3 Different Methods of Providing Microbiological Information

Comparison of the adequacy of antimicrobial therapy during the early period (before intervention). The mean duration ($\pm$SD) of the early period was 4 $\pm$ 1.6 days. The proportion

Table 1. Characteristics of patients in a trial of the impact of different methods of reporting positive blood culture results.

Characteristic	All patients (n = 297)	Group A (n = 109)	Group B (n = 99)	Group C (n = 89)	P
Age, mean years ± SD	62.6 ± 16.9	64.1 ± 17	62 ± 17	62 ± 17	.448
Male sex	193 (65)	68 (62.4)	64 (64.6)	61 (68.5)	.663
Service					.658
Medical	139 (46.8)	53 (48.6)	44 (44.4)	42 (47.2)	
Surgical	69 (23.2)	21 (19.3)	29 (29.3)	19 (21.3)	
Intensive care unit	51 (17.2)	17 (15.6)	15 (15.2)	19 (21.3)	
Hematology-oncology	30 (10.1)	14 (12.8)	9 (9.1)	7 (7.9)	
Other	8 (2.7)	4 (3.7)	2 (2.0)	2 (2.2)	
Microorganisms isolated					.210
Gram positive	185 (54.2)	76 (58.9)	63 (55.8)	47 (47.5)	
Gram negative	133 (39.2)	48 (37.2)	38 (33.6)	46 (46.5)	
Anaerobe	15 (4.4)	1 (0.8)	9 (7.9)	5 (5.0)	
Fungus	8 (2.2)	4 (3.1)	3 (2.7)	1 (1.0)	
McCabe and Jackson classification					.861
Type I	23 (7.8)	6 (5.5)	9 (9.1)	8 (9.0)	
Type II	118 (39.7)	44 (40.4)	38 (38.4)	36 (40.4)	
Type III	156 (52.5)	59 (54.1)	52 (52.5)	45 (50.6)	
Mean Charlson comorbidity score ± SD	3.7 ± 2.5	3.6 ± 2.4	3.8 ± 2.6	3.7 ± 2.4	.876
Predisposing condition or risk factor					
Hypoproteinemia	100 (33.7)	36 (33.0)	33 (33.3)	31 (34.8)	.961
Injection drug abuse	12 (4.0)	3 (2.8)	5 (5.1)	4 (4.5)	.679
Neutropenia	15 (5.1)	8 (7.3)	5 (5.1)	2 (2.2)	.266
Splenectomy	6 (2.0)	1 (0.9)	1 (1.0)	4 (4.5)	.140
Radiotherapy	5 (1.7)	4 (3.7)	0 (0)	1 (1.1)	.107
Chemotherapy	38 (12.8)	19 (17.4)	10 (10.1)	9 (10.1)	.190
Corticosteroid therapy	53 (17.8)	21 (19.3)	20 (20.2)	12 (13.5)	.432
Prior surgery	68 (22.9)	26 (23.9)	20 (20.2)	22 (24.7)	.729
Invasive procedures	134 (45.1)	52 (47.7)	44 (44.4)	38 (42.7)	.770
Prosthetic material	69 (23.2)	23 (21.1)	24 (24.2)	22 (24.7)	.801
Intravenous lines	185 (62.3)	68 (62.4)	58 (58.6)	59 (66.3)	.553
Bladder catheter	95 (32)	29 (26.6)	32 (32.3)	34 (38.2)	.219
Skin lesions	33 (11.1)	16 (14.7)	9 (9.1)	8 (9.0)	.330
Prior antimicrobial therapy	88 (29.6)	36 (33.0)	30 (30.3)	22 (24.7)	.437
Mean APACHE II score ± SD	12.6 ± 5.6	12.6 ± 5.6	12.6 ± 5.9	12.5 ± 5.2	.938
Nosocomial acquisition	157 (54.5)	64 (59.8)	47 (49.0)	46 (54.1)	.299
Portal of entry					.594
Unknown	67 (23.3)	32 (29.9)	20 (20.8)	15 (17.6)	
Urinary or genital	56 (19.4)	18 (16.8)	18 (18.8)	20 (23.5)	
Intravenous catheter	51 (17.7)	18 (16.8)	16 (16.7)	17 (20)	
Respiratory	32 (11.1)	12 (11.2)	11 (11.5)	9 (10.6)	
Biliary	23 (8)	6 (5.6)	11 (11.5)	6 (7.1)	
Cutaneous	24 (8.3)	9 (8.4)	8 (8.3)	7 (8.2)	
Intraabdominal	23 (8.0)	7 (6.5)	9 (9.4)	7 (8.2)	
Surgical wound infection	9 (3.1)	2 (1.9)	3 (3.1)	4 (4.7)	
Central nervous system	3 (1.0)	3 (2.8)	0 (0)	0 (0)	
Organ or system involved					
None	246 (86.3)	93 (88.6)	82 (85.4)	71 (84.5)	.689
Lung	11 (3.9)	5 (4.8)	4 (4.2)	2 (2.4)	.687
Peritoneum/pleural	12 (4.2)	4 (3.8)	6 (6.3)	2 (2.4)	.421
Endocarditis	6 (2.1)	1 (1)	3 (3.1)	2 (2.4)	.551
CNS	2 (0.7)	0 (0)	2 (2.1)	0 (0)	.138
Bone and joint	4 (1.4)	1 (1)	3 (3.1)	0 (0)	.182
Skin	2 (0.7)	0 (0)	1 (1.0)	1 (1.2)	.552
Other	15 (5.3)	5 (4.8)	3 (3.1)	7 (8.3)	.284

NOTE. Data are no. (%) of patients, unless otherwise indicated. Group A, patients whose caregivers received conventional information; group B, patients whose caregivers received conventional information and a written-alert report; group C, patients whose caregivers who received conventional information and both written- and oral-alert reports.

Table 2. Risk factors for inadequate empirical therapy.

Variable	Adequacy if the factor is present	Adequacy if the factor is absent	*P*	OR (95% CI)
Microorganism				
Streptococcus pneumoniae	23/26 (88.5)	147/264 (55.7)	.001	6.1 (1.8–20.8)
Escherichia coli	47/62 (75.8)	123/228 (53.9)	.002	2.7 (1.4–5.1)
Staphylococcus epidermidis and other coagulase-negative staphylococci	17/40 (42.5)	153/250 (61.2)	.026	0.5 (0.2–0.9)
Enterococcus species	10/29 (34.5)	160/261 (61.3)	.005	0.3 (0.1–0.7)
Fungus	1/7 (14.3)	169/283 (59.7)	.016	0.1 (0.0–0.9)
Service				
Nephrology	9/10 (90.0)	161/280 (57.5)	.036	6.6 (0.8–53.2)
Infectious diseases	16/18 (88.9)	154/272 (56.6)	.006	6.1 (1.4–27.2)
Postsurgical intensive care unit	5/15 (33.3)	165/275 (60.0)	.041	0.3 (0.1–1.0)
Underlying disease				
Heart disease	37/77 (48.1)	133/213 (62.4)	.028	0.6 (0.3–0.9)
Neoplasia	24/53 (45.3)	146/237 (61.6)	.029	0.5 (0.3–0.9)
AIDS	16/18 (88.9)	154/272 (56.6)	.007	6.1 (1.4–27.2)
Predisposing condition or risk factor				
Prior surgery	28/67 (41.8)	142/223 (63.7)	.001	0.4 (0.2–0.7)
Invasive procedures	63/129 (48.8)	107/161 (66.5)	.002	0.5 (0.3–0.8)
Intravenous lines	86/182 (47.3)	84/108 (77.8)	<.001	0.3 (0.1–0.4)
Bladder catheter	42/93 (45.2)	128/197 (65.0)	.001	0.4 (0.3–0.7)
Skin lesion	14/32 (43.8)	156/258 (60.5)	.070	0.5 (0.2–1.1)
Prior antimicrobial therapy	41/86 (47.7)	129/204 (63.2)	.014	0.5 (0.3–0.9)
Nosocomial acquisition	69/157 (43.8)	96/128 (75.0)	<.001	0.3 (0.2–0.4)
Portal of entry				
Respiratory	25/32 (78.1)	140/253 (55.3)	.014	2.9 (1.2–6.9)
Urinary or genital	40/55 (72.7)	130/235 (55.3)	.018	2.2 (1.1–4.1)
Septic shock at presentation	71/105 (67.6)	99/185 (53.5)	.019	1.8 (1.1–3.0)

NOTE. Data are *n/N* (%), unless otherwise indicated. Data are provided as adequacy of the antiretroviral therapy, in relationship to the presence or absence of different factors.

of patients who received an antibiotic that was active in vitro against the microorganism responsible for the BSI improved from day 1 to day 5 of the episode (58.5% on day 1, 75.2% on day 2, 83% on day 3, 83.1% on day 4, and 84.4% on day 5; figure 1).

The adequacy of the antimicrobial therapy during the early period by different criteria is summarized in table 4. There was no significant difference in the proportion of days on which appropriate treatment was received among the 3 study groups for any of the parameters considered.

Comparison of the adequacy of antimicrobial therapy during the late period (after intervention). No interventions were applied to group A. Changes in antimicrobial therapy were recommended in group B in 52 cases (52.3%) and in group C in 47 cases (53.1%). Recommended changes were made in 42 episodes (80%) in group B and in 45 episodes (95.3%) in group C. The adequacy of antimicrobial treatment after the final microbiological information was available is summarized in table 5, which compares the 3 different methods of reporting.

Differences in the adequacy of treatment between the early and late periods (considering only the use of antimicrobials with in vitro activity [i.e., coverage]) evolved for the 3 groups as follows: group A, 77.2% to 89%; group B, 78.3% to 98.3%; and group C, 73.6% to 97.1%. In the late period, the adequacy of coverage was significantly different between the 3 groups ($P = .004$). The proportion of days in the late period during which the antimicrobial spectrum was considered to be appropriate was significantly different among the 3 groups (71.1%, 92.1%, and 91.3% for groups A, B, and C, respectively; $P < .001$). Overall, the proportion of days on which adequate treatment was received in the late period was significantly different for the 3 groups (66.3%, 92.1%, and 91.2% for groups A, B, and C, respectively; $P < .001$) (figure 2).

The impact of the different interventions on other parameters for groups A, B, and C were as follows: mean appropriate DDDs during the late period, 16.4, 22.2, and 20.7, respectively ($P = .003$); mean length of hospital stay, 19.8, 23.6, and 24.1 days, respectively ($P = .761$); and mortality rate during the late

Table 3. Relationship between adequacy of empirical treatment and mortality and other clinical variables.

Variable	Adequate treatment received	Inadequate treatment received	*P*	OR (95% CI)
Clostridium difficile–associated diarrhea	3/160 (1.9)	9/109 (8.3)	.013	0.2 (0.1–0.8)
Renal failure during episode	32/153 (20.9)	27/108 (25.0)	.437	0.8 (0.4–1.4)
Shock or multiple-organ failure	7/160 (4.4)	11/109 (10.1)	.065	0.4 (0.2–1.1)
Mortality				
Overall	33/170 (19.4)	37/120 (30.8)	.025	0.5 (0.3–0.9)
Infection-related	23/170 (13.5)	28/120 (23.3)	.031	0.5 (0.3–0.9)
Length of hospital stay, mean days ± SD	19.4 ± 15.8	27.2 ± 32.4	.017	…

NOTE. Data are no. (%) of patients with the variable in groups with adequate or inadequate therapy.

period, 12.9%, 15.6%, and 11%, respectively ($P = .670$). The differences between the groups in mortality rate, duration of hospital stay, and other secondary clinical variables were not statistically significant.

Antimicrobial inappropriateness correlated with large increases in cost. The mean total cost of antimicrobials per episode of BSI was €580.63 (US$707.85) in group A, €537.98 (US$699.73) in group B, and €434.53 (US$529.73) in group C. The mean costs of inappropriate therapy per episode in groups A, B, and C were €138.18 (US$168.45), €39.81 (US$48.53), and €35.98 (US$43.86), respectively ($P < .001$).

Factors that Predict Increased Mortality on Multivariate Analysis

When all of the variables for the different periods were studied by multivariate analysis, the factors that predicted an increased infection-related mortality rate included shock (OR, 8.6; 95% CI, 3.5–21.1; $P < .0001$), *S. aureus* bacteremia (OR, 8.5; 95% CI, 3.5–20.5; $P < .0001$), APACHE II score of >12 (OR, 8.4; 95% CI, 3.2–21.9; $P < .0001$), receipt of inappropriate empirical antimicrobial treatment (OR, 3.5; 95% CI, 1.5–8.2; $P < .003$), and the length of the early period (OR, 1.2; 95% CI, 1.05–1.4; $P = .012$).

DISCUSSION

BSIs represent a good model for assessing the impact of different therapeutic interventions [3, 4, 19–21]. The rate of misuse of antimicrobials for treatment of BSIs has been reported to be 41%–85% of cases, particularly during the empirical period [1, 6, 8, 9, 22–24]. The impact of an adequate initial therapy during the first 24 h of treatment on the evolution of patients with ventilator-associated pneumonia [25] and other severe infections has been well documented, but information regarding its impact on BSIs is scarce [8, 26–28]. Our data show that ineffective empirical therapy has a dramatic impact on the presence of *C. difficile*–associated diarrhea, prolonged length of hospital stay, and mortality. Nosocomial pathogens were risk factors for inappropriate treatment during the empirical period in our study. Because this is a microbiologically "blind" period, it is clear that the solution to the problem depends on continuing medical education and more-efficient microbiological techniques that provide more-rapid indicator for the clinician.

Most institutions report the results of blood cultures in 2 main stages. First, there is an initial emergency report that includes the results of a Gram stain of broth from positive cultures. This is usually followed by a definitive written report,

Table 4. Adequacy of therapy during the early period.

Adequancy parameter	Mean percentage of days during which appropriate therapy was received ± SD				*P*
	Overall	Group A	Group B	Group C	
Indication	93.8 ± 18.0	92.3 ± 20.9	96.7 ± 12.8	92.3 ± 18.8	.123
Coverage	76.5 ± 34.9	77.2 ± 32.5	78.3 ± 34.7	73.6 ± 38.1	.709
Dose	88.3 ± 24.9	88.1 ± 24.6	92.2 ± 20.9	84.4 ± 28.9	.096
Interval	91.9 ± 20.9	90.0 ± 23.7	95.0 ± 15.5	90.8 ± 22.3	.273
Route	89.0 ± 24.9	86.5 ± 29.1	92.6 ± 20.4	88.2 ± 23.7	.243

NOTE. See Definitions for definitions of adequacy parameters. Group A, patients whose caregivers received conventional information; group B, patients whose caregivers received conventional information and a written-alert report; group C, patients whose caregivers who received conventional information and both written- and oral-alert reports.

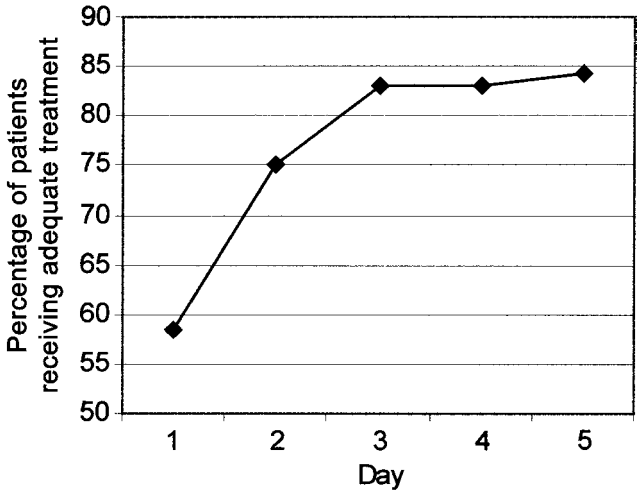

Figure 1. Proportion of patients receiving adequate treatment from day 1 to day 5.

which is made when the microorganism is isolated and the antimicrobial susceptibility test result is known.

To our knowledge, the evolution of the adequacy of antimicrobial therapy during the early period of treatment has not been well studied. Before all of the microbiological data are reported, the results of the Gram stain are already known. The potential benefit of using this information is of enormous value in improving patient outcome. The predictive value of the Gram stain of the pathogens isolated in blood cultures is high [29], especially for *Staphylococcus* and *Streptococcus* species [30]. Performance of a "direct preliminary" antibiogram using blood-broth has not been officially addressed by the American Society for Microbiology [31], despite the fact that it is common practice in many institutions. Published data show a good relationship between the findings obtained using this method and the results of standard definitive antimicrobial susceptibility tests [32, 33]. In their study, Byl et al. [14] found that the report of the Gram stain findings considerably increased the proportion of patients who received appropriate treatment. Our results show that the proportion of patients who received ⩾1 antimicrobial with in vitro activity against bloodstream pathogens increased from 58.5% the first day, to 75% on the second day, and to 83% on the third day. Our data, as well as the data of Byl et al. [14] and others [7], suggest that the "early period" (before the definitive microbiological report is available) could be a critical period for providing information. De-escalation of therapy, as is common practice in patients with ventilator-associated pneumonia, should also be implemented for patients with suspected BSI.

Despite these efforts to provide information, some authors warn about the worrying limited value of written laboratory reports, because 8%–20% of patients are still inappropriately treated after the pathogens and their susceptibility patterns are known [4, 5, 8, 10, 11, 28].

Our study tried to assess the complementary value of 2 different means of making information available to the clinician at a specific moment in the evolution of cases during the "late period" of treatment. We compared use of the classic procedure (group A) with receipt of an additional written report with recommendations (group B) or written and oral reports with recommendations (group C) at the bedside.

Active notification led to suggestions regarding alteration of therapy in ~50% of cases, as occurred in previous studies [6, 13]. The improvement in treatment was significantly greater for patients whose blood culture results were accompanied by written- or oral-alert reports. Patients in the conventional information group received appropriate treatment for a mean of only 66% of the duration of the episodes, whereas patients in the active information groups were correctly treated for a mean of 92% of the duration. Active notification of blood culture results also led to a significant reduction in cost, with savings of ~25% per episode (taking into consideration only the cost of purchasing of drugs).

Our data clearly show that the delay until the final microbiological report becomes available is an independent risk factor for infection-related mortality: the risk of death increases 1.2-fold for each day until definitive microbiological information is available. Nevertheless, our study failed to demonstrate that our 2 procedures for active notification of blood culture results had a direct impact on postintervention duration of hospital stay or mortality. In our opinion, this is because these recommendations usually arrive >4 days after blood samples are obtained for culture, pointing to a probable need for earlier interventions and advice based only on the preliminary information available. This information should be conveyed by an infectious diseases specialist or a clinical microbiologist. A recent study of patients with bacteremia and pneumonia in an

Table 5. Adequacy of therapy during the late period.

Adequacy parameter	Mean percentage of days during which appropriate therapy was received ± SD			
	Group A	Group B	Group C	*P*
Indication	91.3 ± 22.1	98.6 ± 6.2	98.6 ± 9.8	.001
Coverage	89.0 ± 27.3	98.3 ± 6.4	97.1 ± 14.0	.004
Dose	88.6 ± 27.6	98.6 ± 6.2	98.1 ± 10.6	.001
Interval	90.1 ± 25.8	98.6 ± 6.2	98.2 ± 10.6	.002
Route	88.0 ± 27.8	98.6 ± 6.2	98.4 ± 9.8	<.001
Spectrum	71.1 ± 42.0	92.1 ± 23.6	91.3 ± 23.1	<.001
Overall	66.3 ± 43.7	92.1 ± 23.6	91.2 ± 23.1	<.001

NOTE. See Definitions for definitions of adequacy parameters. Group A, patients whose caregivers received conventional information; group B, patients whose caregivers received conventional information and a written-alert report; group C, patients whose caregivers who received conventional information and both written- and oral-alert reports.

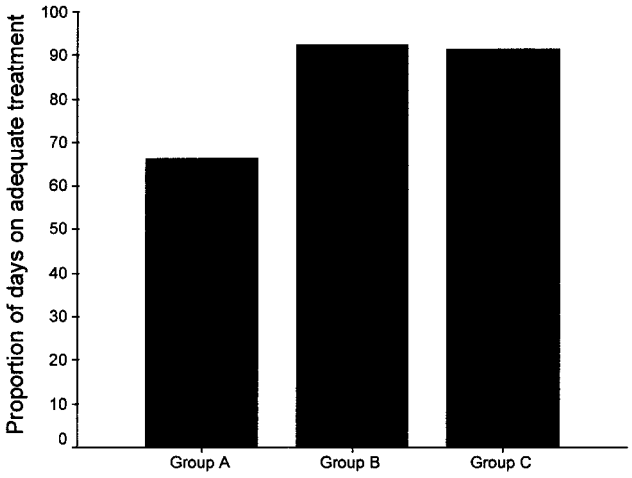

Figure 2. Proportion of days of adequate treatment during the "late period" in each group.

intensive care unit demonstrated that adequate antibiotic treatment only had an impact on survival if it was started within the first 24 h after samples were obtained ($P < .02$ on day 0 and $P < .04$ on day 1) [26].

In conclusion, our data emphasize the importance of the early availability of microbiological information to improve the outcome of severely infected patients. They also underline the clinical and economic benefits of close coordination between the laboratory and clinicians for interpretation of microbiological information and for making decisions on therapeutic procedures. New complementary methods of reporting blood culture results, which can contribute to the optimal care of patients with BSI, should be introduced.

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