Earlier Initiation of Antibiotic Treatment for Severe Infections After Interventions to Improve the Organization and Specific Guidelines in the Emergency Department

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Objective: To examine whether combined interventions improve the timely administration of antibiotic therapy and acquisition of material for culture from patients admitted to the emergency department with a serious infectious disease.

Methods: Guidelines and educational programs were developed to facilitate timely antibiotic administration: guidelines on handling patients with serious infections and on ordering immediate treatment, guidelines on obtaining culture samples, lectures to medical and nursing staff, improvement of availability of antibiotics in the emergency department, and removal of financial restraints on stocking and ordering of antibiotics. Fifty consecutive patients were evaluated after this series of interventions and compared with the results in 50 patients evaluated before the interventions. The interval from presentation to the emergency department until the administration of antibiotics, number of samples taken for microbiological investigations, and number of patients receiving a first dose of antibiotic at routinely scheduled drug distribution rounds were evaluated.

Results: The median time to the initial dose of antibiotics administered decreased from 5.0 hours to 3.2 hours (P = .04). The number of blood cultures obtained did not change. The percentage of sputum cultures obtained increased from 28% to 50%, and the percentage of urine cultures obtained increased from 50% to 100%. The percentage of patients whose first dose of antibiotic was delayed until a routinely scheduled drug distribution round decreased from 54% to 32% (P = .03).

Conclusions: Combined interventions to expedite diagnostic and therapeutic actions through directed clinical practice guidelines and organizational measures are successful. This may lead to a substantial quality improvement in the process of care.

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The acquisition of material for culture and the timely administration of effective antibiotic therapy are widely viewed as basic to the treatment of patients with serious infections. However, with the exception of studies in patients presenting with bacterial meningitis, few data are available that describe these processes.1,2

In a previous study, we analyzed the interval from the time of admission to the emergency department (ED) until the administration of antibiotics in patients suspected of having a serious infection needing immediate empirical antibiotic treatment.3 We found a median delay of 5.0 hours (range, 0.6-13.3 hours) before patients received their first dose of antibiotics. A step-by-step analysis revealed that this delay depended on several factors.

Whereas the clinical presentation, the type of infection, or the collection of cultures did not influence the delay in the start of therapy, we found that extensive evaluation of the patient by residents and senior staff was a main cause for delay.3 In addition, the transfer of the patient from the ED to the ward often leads to repeated diagnostic procedures and delay of therapeutic measures. Finally, despite written orders to start antibiotic therapy, nurses tended to delay the administration of antibiotics until routinely scheduled drug distribution rounds fixed by the nursing staff, mainly at 6 PM and 12 PM.3

The objective of the present study was to conduct a series of educational and organizational interventions, and to reevaluate the management of patients admitted to the hospital with serious infections, after implementing these interventions designed to improve the process of care. A combined approach was chosen to analyze the barriers to change and implement multiple interventions to change the performance of the health care practition-
PATIENTS AND METHODS

STATEMENT OF THE PROBLEM

In our previous study we identified a number of causes for the delay in administering antibiotics to patients with serious infections. Obstacles were the belief that patients should be fully evaluated before taking any action, the belief that blood cultures should only be taken with a body temperature above 38.5°C, and that antibiotics were not readily accessible in the ED; hence, patients were transferred to the ward before starting treatment. On the ward, nurses often thought they could wait until the next scheduled drug distribution round for administration of the prescribed antibiotic.

DATA COLLECTION

A prospective survey of medical records and prescription charts was performed at the Division of General Internal Medicine of the University Hospital Nijmegen, Nijmegen, the Netherlands. Fifty patients admitted to the ED and presumptively diagnosed as having a serious infection that required immediate empirical antibiotic treatment were recruited for the study, as described previously. After analysis of the barriers to change and subsequent intervention, another 30 patients consecutively admitted to the ED with a presumptive diagnosis of serious infection were analyzed.

INTERVENTIONS

On the basis of the analysis, guidelines and educational programs were developed to facilitate timely antibiotic administration. The interventions performed are summarized below.

• Newsletter to the medical staff informing about the observed delay
• Guidelines on managing patients with presumed serious infections and on ordering immediate treatment
• Guidelines on obtaining cultures for microbiological analysis
• Lectures to the medical staff
• Lectures to the nursing staff

• Improvement of the availability of antibiotics in the ED in a readily accessible place
• Removal of financial restraints on stocking and ordering antibiotics in the ED

The guidelines determine that antibiotics are administered in the ED immediately after taking cultures, not waiting for the next routinely scheduled drug distribution round. Two sets of blood cultures should be taken irrespective of the patient's body temperature. A urine sample and/or a sputum sample, if necessary after induction of sputum with isotonic sodium chloride solution should be collected, where appropriate. The collection of cultures may not delay the administration of antibiotics.

In educational sessions, the guidelines were introduced to all medical officers of the department. The nurses of the infectious diseases ward were taught about the measures.

In discussions with the head of the ED various organizational problems concerning the administration of antibiotics were solved such as the funding of the antibiotics needed, the stocking in a readily accessible place, and the ordering process from the pharmacy.

OUTCOMES

The outcomes measured were variables to define the appropriateness of the procedure of initiating antibiotic treatment and to assess the quality of the provided health care services; the interval from presentation to the ED until the administration of antibiotics, subdivided into day, night, or weekend shift; the source and number of samples taken for microbiological investigations; the relation between body temperature at admission and collection of culture samples; and the number of patients receiving their first dose of antibiotic at routinely scheduled drug distribution rounds. Furthermore, length of stay and in-hospital mortality was assessed.

STATISTICAL ANALYSIS

P \leq .05 was considered statistically significant. The Mann-Whitney U test was used to compare the time intervals between the 2 groups of patients. The \chi^2 test was used to test categorical variables. Where indicated, data are given as mean ± SD.

RESULTS

The patient characteristics are summarized in Table 1. There was no difference between the groups studied before and after the interventions with regard to baseline characteristics.

The median time from admission to the initial administration of antibiotics was 5.0 hours (range, 0.6 to 13.3 hours) for all 50 patients before the interventions. This decreased significantly to 3.2 hours (range, 0.6 to 10.5 hours; \( P = .04 \)) after the interventions (Table 2). Whereas before the interventions the interval was significantly longer in patients admitted during office hours than in patients admitted at night (6.1 ± 3.2 hours vs 3.7 ± 1.9 hours; \( P = .03 \)), this difference was no longer significant after the interventions (3.3 ± 2.8 hours vs 2.8 ± 1.9 hours; \( P = .39 \)). The percentage of patients whose first dose of antibiotic was delayed to a routinely scheduled drug distribution round decreased from 54% to 32% (\( P = .03 \); Table 2).

No differences were found in the total number of blood cultures taken before or after the interventions. However, of the patients presenting with a respiratory tract infection, a sputum culture before starting antibiotic treatment was obtained from 5 (28%) of 18 before
and 12 (50%) of 24 patients after the interventions \((P = .15)\). In the case of presumed urinary tract infection, a urine culture was obtained from 6 (50%) of 12 patients before the interventions and in 100% of the patients after the interventions \((P = .16)\).

More blood cultures were obtained from patients with a high temperature at admission. Before the interventions, the peak temperature of patients with 2 or more blood cultures was \(38.8^\circ C \pm 1.0^\circ C\) compared with \(37.8^\circ C \pm 1.2^\circ C\) for those with none or 1 set of blood cultures \((P = .02)\). After the interventions, the same pattern existed \((38.9^\circ C \pm 1.2^\circ C\) vs \(38.2^\circ C \pm 0.9^\circ C; P = .03)\). The mean length of stay decreased from 19.1 ± 17.2 days before the interventions to 14.7 ± 12.4 days after the interventions \((P = .05)\). The in-hospital mortality (4%) did not change after the interventions.

**COMMENT**

In the present study we have shown that interventions to expedite the timely performance of key diagnostic and therapeutic actions through directed clinical practice guidelines are successful. Efforts to identify and minimize common barriers significantly improved the timing of antibiotic administration. A combination of written and oral interventions was performed to educate the medical and nursing staff involved in the treatment of these patients.

The findings of the present study are in agreement with a vast body of research on medical education strategies. Whereas interventions and conventional medical education programs have little effect, multifaceted interventions have been shown to be particularly effective. Such strategies should concentrate on already developed and generally approved guidelines, and be targeted at specific behaviors identified by a gap analysis and audit addressing specific shortcomings and barriers to change.3,9 The present study has specifically focused on these types of intervention, which may have contributed to the favorable outcome.

The interventions in this study have improved the percentage of patients who had urine or sputum cultures taken when the focus of infection was thought to be the urinary or respiratory tract.

The practice of obtaining blood cultures could not be changed with the present interventions. The precaution that blood cultures are only of value if the patient presents with a body temperature above 38.5°C still appears to be widespread. This observation should lead to a further intervention, since it has been shown that there is little correlation between the presence of fever at admission and culture-proven sepsis.10

Limited data are available in the literature describing these types of interventions. Guidelines on initial antibiotic treatment only incidentally contain advice on the timing of treatment.11-13 Reports of delays in administering antibiotics vary considerably between 3.5 hours and 12.8 hours.14-18 Blood cultures have been taken in 34% to 81% of the patients14,16-18 and sputum cultures in 22% to 70%.14,16,18

Only a few published studies have shown an improvement of the variables studied after interventions. One study reports a reduction of the interval between admission and administration of antibiotics by about 3 hours.19 Other authors report that more patients received the antibiotic within 4 hours20 or that more patients received antibiotics in the ED after intervention.21 In a study on the reduction in mortality from pneumonia, a series of interventions consisting of written and oral information on the performance of the therapeutic interventions in the ED led to an increase in the percentage of patients receiving their first dose of antibiotic within 4 hours of admission from 42% to 87% and reduction of the mortality rate from 10.2% to 6.8%.22 In one retrospective study of patients with urinary tract infections,23 a significant reduction in the mean length of stay was seen comparing patients whose antibiotics were administered within 4 hours of admission vs those whose antibiotics were administered outside the 4-hour frame.

The present study was aimed at behavioral change rather than assessing patient outcome, and although there was a trend toward shorter hospital stay after the interventions, the number of patients is not appropriate to statistically evaluate such effects. Nevertheless, the significant improvement in the process of care is considered crucial in improving outcome.22,23 Attention to the process of care, in addition to its content, is important in assessing the need for formulation of institutional practice guidelines. Coordination of care in the ED and on the inpatient ward with contributions from the pharmacy and the laboratory is necessary to modify key as-

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Before Interventions ((n = 50))</th>
<th>After Interventions ((n = 50))</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, M/F</td>
<td>22/28</td>
<td>30/20</td>
<td>.11</td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>64 ± 19</td>
<td>63 ± 19</td>
<td>.25</td>
</tr>
<tr>
<td>Aged &gt;60 y, No. (%)</td>
<td>30 (60)</td>
<td>34 (68)</td>
<td>.40</td>
</tr>
<tr>
<td>Diagnosis, No. of patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>18</td>
<td>24</td>
<td>.22</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>12</td>
<td>5</td>
<td>.06</td>
</tr>
<tr>
<td>Erysipelas</td>
<td>8</td>
<td>3</td>
<td>.11</td>
</tr>
<tr>
<td>Fever and neutropenia</td>
<td>2</td>
<td>3</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Septicemia</td>
<td>10</td>
<td>15</td>
<td>.25</td>
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</tbody>
</table>

### Table 2. Administration of Antibiotics

<table>
<thead>
<tr>
<th>Delay between admission and antibiotics, median ± SD, h</th>
<th>Before Interventions</th>
<th>After Interventions</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>5.0 ± 2.9</td>
<td>3.2 ± 2.5</td>
<td>.04</td>
</tr>
<tr>
<td>During office hours</td>
<td>6.1 ± 3.2 (n = 15)</td>
<td>3.3 ± 2.8 (n = 23)</td>
<td>.06</td>
</tr>
<tr>
<td>At night</td>
<td>3.7 ± 1.9 (n = 22)</td>
<td>2.8 ± 1.9 (n = 17)</td>
<td>.22</td>
</tr>
<tr>
<td>During weekends</td>
<td>5.0 ± 3.4 (n = 13)</td>
<td>4.5 ± 2.3 (n = 10)</td>
<td>.49</td>
</tr>
<tr>
<td>Antibiotics delayed until routine drug rounds, No. (%) of patients</td>
<td>27 (54)</td>
<td>16 (32)</td>
<td>.03</td>
</tr>
</tbody>
</table>
pects of management, such as reducing the time to initiate antibiotic treatment. This may lead to a substantial improvement of quality in patient care.

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