Improving antibiotic use in the hospital: Focusing on positive blood cultures is an effective option

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Résumé

Amélioration de l’utilisation des antibiotiques à l’hôpital à partir des hémocultures positives

Objectifs > Un avis systématique mais non sollicité donné par l’infectiologue sur les hémocultures positives a été évalué, en utilisant une alerte informatisée à partir du laboratoire de microbiologie. Les principaux objectifs étaient d’améliorer l’usage des antibiotiques pour le traitement des bactériémies et d’arrêter les antibiothérapies non justifiées des hémocultures contaminées.

Méthodes > Pendant la première partie de l’étude (quatre mois), toutes les hémocultures provenant des services de médecine, chirurgie et réanimation ont été évaluées. Après avoir effectué une analyse intérimaire, seules les hémocultures positives de médecine et chirurgie ont été ensuite évaluées pendant la deuxième partie (huit mois).

Summary

Objectives > The unsolicited and systematic evaluation of positive blood cultures (pBC) after laboratory report by a single infectious disease specialist (IDS) was evaluated during one year, using a computer-generated alert by the laboratory. The main objectives of IDS counselling were to improve antibiotic use for bloodstream infection (i.e., initiating or modifying therapy) and to stop unjustified therapy for contaminated pBC.

Methods > During the first part of the study (4 months), all pBC in patients from ICUs, medical and surgical wards were analyzed. After an interim analysis, only pBC from medical and surgical wards were evaluated during the second part (8 months).

Results > Overall, 1090 episodes of pBC (representing 866 patients) were evaluated and classified as bloodstream infection (65.5%), contamination (29%) or undetermined (5.5%). Forty-three percent of episodes prompted IDS counselling,
Blood cultures are an important area for improving the quality of care of patients. A positive blood culture (pBC) may represent bloodstream infection, which requires prompt and adequate antimicrobial therapy, or contamination possibly leading to unnecessary therapy or diagnosis procedures [1–3]. Results of blood cultures are reported to the physician in charge of the patient by the laboratory, with or without therapeutic counselling. However, report and counselling may be inefficient, because the ward physician may be difficult to contact or reluctant to follow counselling or hospital guidelines [4–6].

Complementary advice offered by infectious disease specialist (IDS) to physicians has been shown to improve the care of patients having bloodstream infection, resulting in quicker prescription of more appropriate treatment and improvement of clinical outcome of patients [7–9]. However, the feasibility and potential impact of unsolicited and systematic evaluation by IDS after laboratory report have not been precisely evaluated.

Our goal was to determine whether a systematic but unsolicited evaluation of pBC using a computer-generated alert could be implemented in a large hospital with limited IDS resources. During a 12-month period, we identified hospitalized patients with pBC and offered counselling with the objectives to improve antibiotic use for patients with bloodstream infection or withdraw unjustified therapy for those patients with contaminated pBC.
Methods

Setting
Albert-Chenevier-Henri-Mondor hospital is a tertiary care, 1300-bed university hospital (including five intensive care units [ICU], 13 acute medical, seven surgical and five rehabilitation or long-term care [R-LTC] wards) with an average of 36,000 admissions of adult patients per year. Advices about infectious diseases are provided by only one full-time IDS on an on-call basis in all the departments of the hospital. The same IDS also performed unsolicited post-prescription review of selected antibiotics in surgical and medical wards using a computer-generated system alert that has been described [10]. Hospital antibiotic guidelines issued by the Anti-Infective Drugs Committee are distributed hospital-wide in a format pocket and are also available on the Intranet. Every 6 months, all staff and junior physicians of each ward are offered educational sessions about antibiotic prescribing. Preliminary reports of pBC, notably Gram stain results, are reported twice a day by the microbiology laboratory by phone to the attending physicians and are usually associated with an initial therapeutic counselling when judged appropriate. Preliminary and definitive results of blood culture (including species identification and susceptibility results) are later available on the Intranet.

Programme design
A computer-generated alert based on laboratory results was made available to the IDS since November 2008, allowing screening of all positive pBC. The alert gave the identity and location of the patient, date of sampling of the pBC, Gram stain result, on the same day that the physician in charge was informed by phone of the positivity of the BC and Gram Stain result. After testing the system for one month, we developed a timeline for IDS intervention as follows: during the first 4-month period of the study (December 2008 to April 2009), all hospital wards (except the bone marrow transplantation unit) were surveyed. The IDS checked the pBC listing everyday (except on week end) in the afternoon. Antimicrobial therapy prescribed in the corresponding medical, surgical and R-LTC wards was screened the same day using the computerized prescription system implemented in our hospital since 2005. When judged necessary, the attending physician was called by phone or visited by the IDS. The next day, at the time of identification and susceptibility results that were usually available on the Intranet, every pBC whatever the ward was evaluated by the IDS by ward visit and direct interaction with the attending physician. At the end of this period, we performed an interim analysis of IDS interventions. During the following 8-month period (May to December 2009), the intervention was restricted to any pBC in medical, surgical and R-LTC wards using the same method as described above.

Whatever the period of the study, the main objectives of the IDS intervention were to provide counselling for the most adequate antibiotic therapy for patients with bloodstream infection and, whenever possible, to withdraw unnecessary therapy for pBC considered as contaminated. We followed the recommendations of the STROBE statement for reporting the results of observational studies. Our institutional ethics review committee approved the study protocol and waived the requirement for informed consent.

Bloodstream infection
Each pBC was evaluated to determine whether it more likely represented bloodstream infection or contamination, on the basis of available clinical and microbiological data. In the interpretation of blood cultures growing potential contaminants arising from the skin micro flora, such as coagulase-negative *Staphylococcus* or *Corynebacterium* species, at least two pBC for the same microorganism (i.e., identical in terms of species and antimicrobial susceptibility profile) were required in association with clinical manifestations of infection and no other explanation before a diagnosis of bloodstream infection was considered [11]. A pBC episode was defined by the first pBC or by a new pBC occurring more than 7 days after a previous episode [12].

Criteria for infectious disease specialist counselling
The IDS interventions were categorised as follows:
- **Initiation:** when the IDS advised initiation of antimicrobial therapy (including selection of the agent, route of administration, dosage and duration) for a pBC considered as a true bloodstream infection in a patient having no ongoing antimicrobial therapy;
- **Modification:** when the IDS recommended changing an ongoing antimicrobial therapy (including change of antibiotic spectrum, oral switch, dosage and planned duration of therapy);
- **Withdrawal:** when the attending physician was strongly encouraged to withdraw antimicrobial administration for a contaminated pBC;
- **Diagnosis:** when recommendations for performing diagnostic or monitoring tests were provided by the IDS.

Statistical analysis
The unit of the analysis was the episode of positive BC and not the patient (patients could be enrolled twice if there was an interval of at least one week between two episodes). Descriptive statistics are presented as numbers and percentages for categorical variables or median and 25th and 75th percentiles for continuous variables. Differences in IDP counselling between the two periods of the study were compared using the Chi-square or Fisher exact tests, where appropriate. A $P$ value < 0.05 was considered as significant.
Results

Description of pBC

During the 12-month period of the study, 1090 pBC episodes were evaluated by the IDS, corresponding to 866 patients (mean age, 63 ± 14 years): 569 episodes (in 419 patients) were evaluated during the first period and 521 episodes (in 447 patients) were evaluated during the second period. Overall, 1560 pBC episodes were detected by the microbiology laboratory during the whole period of the study. The coverage rate of our system was 70%.

During the first period of the study, pBC episodes assessed mainly originated from medical (291/569, 51%) or ICU (204/569, 36%) wards. Few pBC episodes were evaluated in surgical (51/569, 9%) or R-LTC (23/569, 5%) wards. Exclusion of pBC episodes from ICU wards during the second period of the study mainly increased the rate of episodes assessed from medical wards (415/521, 79.5%), whereas surgical (68/521, 13%) or R-LTC (38/521, 7.5%) pBC episodes accounted for a small proportion.

Interpretation of pBC

Of the 1090 episodes evaluated, a total of 716 (65.5%) were considered as bloodstream infections, 316 (29%) were judged as contamination and 58 (5.5%) were considered of undetermined significance. Comparison of the two periods of the study showed that more pBC episodes were considered as bloodstream infection during the second period (374/521, 71.5%; vs. 342/569, 60%; P < 0.001), whereas episodes of undetermined significance accounted for a smaller proportion (9/521, 1.7%; vs. 49/569, 8.6%; P < 0.001). Contaminated pBC represented 178/569 (31.3%) and 138/521 (26.5%) pBC episodes during the first and second periods (P = 0.08).

Distribution of microorganisms isolated from pBC

Overall, the distribution of microorganisms identified was as follows: coagulase-negative staphylococci, 31.9%; Enterobacteriaceae, 29.3%; streptococci, 11.9%; Staphylococcus aureus, 8.4%; Pseudomonas aeruginosa, 3.5%; anaerobes, 2.2%; fungi, 0.8%; others, 4%; and polymicrobial episodes, 5.9%. The relative distribution of microorganisms identified during the two periods of the study is shown in Table I.

Infectious disease specialist counselling

Overall, 477 pBC episodes (43.7%) prompted counselling, but the counselling rate was significantly higher when the evaluation was restricted to medical, surgical and R-LTC wards (319/521, 61.2%) than during the first period of the study (158/569, 27.7%) (P < 0.001). The distribution of interventions was as follows: modification of ongoing antimicrobial therapy, 334/1090 (30.6%); initiation, 58/1090 (5.3%); diagnosis, 56/1090 (5.1%) and withdrawal, 39/1090 (3.5%). Among the modifications suggested by the IDS, the most frequent was...
de-escalating (149/1090, 13.6%), whereas broad-spectrum antibiotic (57/1090, 5.2%), oral switch (46/1090, 4.2%), decreasing the duration (39/1090, 3.5%), dosage (35/1090, 3.2%) or increasing the duration (8/1090, 0.7%) were less frequently counseled. The large majority (90%) of IDS counselling was followed by the attending physicians.

Comparison of IDS counselling between the two periods showed that restriction of the evaluation to medical, surgical and R-LTC wards was more effective, resulting in a higher rate of initiation, withdrawal and modification of ongoing therapy (Table II). More precisely, antimicrobial use after IDS counselling improved during the second part of the study with regard to de-escalating therapy, oral switch and reduction of the planned duration of therapy.

**Discussion**

Determination of the appropriate therapy for bloodstream infections is one of the most common difficulties encountered by physicians in clinical practice [2,12]. This is of paramount importance, because inappropriate therapy has been shown to be associated with worst outcomes, including higher overall or infection-related mortality rates, longer hospital stay and increased costs of therapy [4,11]. Several studies have reported that the rate of appropriate therapy ranged from less than 60 to 85% in this setting [2,5,7,12].

Early reporting blood culture data, notably the results of the Gram stain, is therefore of value in improving patient outcome, because this occurs during the early period of treatment [7]. In many hospitals, this is usually done by the microbiology laboratory by a phone call to the ward. However, this report remains problematic for many reasons: the treating physician may not always be aware of the results because the information is not transmitted or lost or he/she may be not familiar with the potential diagnostic and therapeutic problems encountered in the management of bloodstream infections. There is no question that ID or clinical microbiologist is the main actor to assure a proper liaison between the laboratory and the treating physicians, because several studies have shown that these advices optimized patient care and decreased antibiotic and side effect related costs [7–9,11,13]. The importance of close coordination between the microbiology laboratory and the ID team has been emphasized, and it has been shown that written- or oral-alert reports associated with clinical advice should complement traditional microbiological reports for patients with bloodstream infections [11]. The question that remains to be answered is how to facilitate and optimize the IDS advice in the ‘decision-making loop’, because in many

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Period 1 (n = 569)a</th>
<th>Period 2 (n = 521)b</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Any counselling</td>
<td>158 (27.7)</td>
<td>319 (61.2)</td>
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<td>Withdrawal</td>
<td>11 (1.9)</td>
<td>28 (5.3)</td>
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<td>Initiation</td>
<td>12 (2.1)</td>
<td>46 (8.8)</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Modification</strong></td>
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<tr>
<td>De-escalating</td>
<td>46 (8.0)</td>
<td>103 (19.7)</td>
<td>&lt;0.001</td>
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<td>Broad-spectrum</td>
<td>29 (5.1)</td>
<td>28 (5.3)</td>
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<tr>
<td>Oral switch</td>
<td>13 (2.3)</td>
<td>33 (6.3)</td>
<td>&lt;0.001</td>
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<tr>
<td>Decreasing the duration</td>
<td>11 (1.9)</td>
<td>28 (5.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>Increasing the duration</td>
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<td>Dosage</td>
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<td>20 (3.8)</td>
<td>0.26</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>39 (6.8)</td>
<td>27 (5.2)</td>
<td>0.24</td>
</tr>
</tbody>
</table>

*a Episodes identified in intensive care unit (ICU), medical, surgical and rehabilitation or long-term care (R-LTC) wards.

*b Episodes identified in medical, surgical and R-LTC wards.
hospitals IDSs are called too late or are not informed of the pBC results and their resources are scarce. We believe that the situation in place in our hospital for many years before performing this study is commonly observed in other institutions, marked by limited IDS resources given the hospital activity and absence of IDS interventions in the management of patients with pBC. This was explained by the fact that IDS advices originating mainly from voluntary calls of wards physicians or post-prescription review of selected antibiotics. Particularly, there was no close coordination between the microbiology laboratory and the IDS for the management of pBC. In the early and mid 2008, we observed two cases of severe hospital-acquired *S. aureus* bloodstream infections that were not adequately managed despite early report of pBC and therapeutic advice by the laboratory, resulting in fatal outcome for one patient. This prompted the hospital administration and medical staff leadership to support the implementation of the computer-generated alert, which was judged as an important component of patient safety [14]. The alert implemented for the systematic evaluation of pBC was very simple and gave only limited but helpful data, such as positive Gram results (including arrangement of the organisms), time between sampling and positivity and number of pBC [3,15]. We also took advantage of implementation of the computerized prescription system implemented in surgical and medical wards 5 years ago and the recent experience of the unsolicited post-prescription review of selected antibiotics using a computer-generated system alert [10]. This investigation showed that the computer-generated alert led the IDS to give unsolicited advices for the management of 43% of pBC and that the large majority of treating physicians accept the counselling, although they did not request it. Recommendations for changes in therapy were in the range of other studies but physicians’ compliance to IDS advices was high [11,13]. This is an important result because previous studies have shown that failure to follow IDS recommendations is a predictor of worst clinical outcome in *S. aureus* bacteremia [9]. Interestingly, modification of ongoing antimicrobial therapy was the most frequent advice, illustrating that IDS advice complemented and did not substitute the initial advice provided by the microbiology laboratory. De-escalating therapy was the most frequent changed proposed for ongoing therapy, demonstrating that a substantial number of patients remained on excessively broad-spectrum antibiotics, a finding that has been previously described [8,13]. Although initiating therapy was less frequently a reason for counselling, 5% of pBC were not treated before the IDS visit despite laboratory report and advice. This finding emphasized the role of the IDS to convey the information delivered by the laboratory to the treating physicians in some cases. Finally, modification of therapy also included withdrawal, oral switch and changing the duration, factors that are associated with the improvement of antibiotic use in hospitals [14].

Restriction of IDS advices in surgical or medical wards during the second part of the study gave useful additional results. As compared to the generalized evaluation performed in the first part, which was successfully initiated but was time consuming, restriction enhanced the impact of the IDS. This was associated with higher rates of bloodstream infections episodes evaluated and more IDS advices, including initiation, withdrawal and other important components of antibiotic use (de-escalating, oral switch or reducing duration). Reasons for such a difference remained unclear. Comparison of pBC of undetermined significance (as assessed by the IDS) suggested that interpretation of pBC was easier in non-ICU wards. On the other hand, the IDS may be more reluctant to give advices in ICU wards for other reasons, including severity or complexity of ICU patients. Finally, there are some differences in the ability of physicians with regard to the management of infected patients between ICUs and medical or surgical wards in our hospital: senior physicians are usually involved for the former while residents are in charge for the latter. However, this finding may not be applicable in other hospital settings because studies have shown that a substantial number of patients are still treated inappropriately or received excessively broad-spectrum antibiotics in the ICU [6].

There are some limitations to this study. First, we did not evaluate the clinical impact of the IDS interventions because we did not consider that a randomized trial would be judged ethical. However, positive impact of IDS interventions has been published elsewhere [7-9,11]. Given the high rates of IDS advices and physicians compliance observed in this study, we can hypothesize that a positive impact was observed. Second, this evaluation took place in a hospital setting where solicited or not solicited IDS advices performed by the same physician were in place for several years. This could explain the high rate of observed compliance by the treating physicians but could limit the generalization of our results in other settings. Finally, limited local resources and restriction of IDS evaluation during the second part of the study resulted in moderate (70%) coverage rate of pBC. This was mainly a consequence of the restriction decision after we performed an interim analysis showing that IDS interventions were more effective in non-ICU wards.

In conclusion, these data demonstrate that a systematic evaluation of pBC may be usefully performed by IDS using a computer-generated alert, in addition to the early report of microbiological information by the laboratory. Despite limited resources, the IDS may be able to counsel the treating physicians with a high rate of compliance, suggesting that this strategy may be implemented successfully in many hospitals.

*Conflict of interest*: none
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References


