European Journal of Clinical Microbiology & Infectious Diseases (2019) 38:973–975
https://doi.org/10.1007/s10096-019-03544-9

ORIGINAL ARTICLE

A prospective study on the effect of time-shifted telephone reporting of blood culture microscopy

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Received: 7 March 2019 / Accepted: 18 March 2019 / Published online: 25 March 2019

Abstract

Even though dealing with septic patients, the communication of the Gram stain result of positive blood cultures is postponed in most laboratories outside of conventional working hours. There is little evidence from clinics that this issue is being addressed. This study evaluates the potential benefit of an around-the-clock communication. Therefore, the effect of the communication on the antibiotic treatment and the delay of the communication during our non-office hours were measured. Over a three-month period, all blood cultures which were positive for the first time outside the normal working hours were analyzed. Two standardized telephone calls were used to compare the antibiotic treatment before and after the communication of the Gram stain result. The evaluation of the antibiotic treatment was based on the final testing result. In total, 135 patients were included. The rate of the adequate antibiotic increased by 8 percentage points to 69%. The average delay in the patients adjusted to an adequate treatment was 8:57 h (range 2:16–16:59). This prospective study shows a benefit of the immediate communication. Nevertheless, this benefit seems to be partly the result of suboptimal adherence to the guidelines regarding empirical antibiotic treatment. This prospective study has been registered in the German Clinical Trials Register under the identifier DRKS00014996 (http://www.drks.de/DRKS00014996).

Keywords Blood culture · Antibiotic treatment · Gram stain · Microscopy · Communication

Introduction

An early adequate antibiotic treatment is key to reduce mortality in septic patients [1]. To ensure that the antibiotic treatment is adequate, a blood culture diagnostic is necessary to identify the pathogen and its resistance to antibiotics. Commonly, this takes between 12 and 48 h after a blood culture flagged positive [2, 3]. To get relevant information as fast as possible to the physician in charge, the pathogen in question is Gram stained and classified under the microscope. Although the information is still incomplete at this stage, it could provide early and useful information to adjust the empirical treatment. Outside of conventional working hours, this process is delayed until the next morning in most laboratories due to limited human resources. There is conflicting evidence if around-the-clock diagnostics improve the antibiotic treatment sufficiently to balance the inevitable resource implications [4–7].

The aim of this study was to evaluate the benefit of an immediate reporting of the microscopic Gram classification, irrespective of the benefit of an immediate processing of the blood culture. Therefore, we investigated the impact of a delayed report outside our normal working hours in all patients with first-time positive blood cultures at a maximum-care hospital. The main objectives were how often and for how long on average the absence of reporting during our non-working hours delayed the adequate antibiotic treatment.

Materials and methods

This prospective study was conducted at the University Hospital Bonn in Germany with 50,000 admissions per year. The period of the study was from June to August 2018. Eligible for participation in the study were all adults over 18 years who were treated in a stationary setting and whose blood culture was positive for the first time outside

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our normal working hours (Monday-Friday 7:30–19:30, Saturday 7:30–15:00, and Sunday 10:00–14:00). Patients that showed no pathogen in the microscopy of the first positive blood culture as well as patients with a palliative care setting were excluded. The study protocol included the standard sample processing, a first phone call, a second phone call, and the interpretation of the antibiotic treatment based on final testing results.

The standard sample processing required that all blood cultures becoming positive during non-working hours were processed the following morning (Monday–Saturday 8:00–9:00 and Sunday 10:00–11:00). The Bactec FX (Becton Dickinson) blood culture system was used for incubation and the automated Poly Stainer (IUL) was used for Gram staining.

The two phone calls allowed identifying adaptations of the antibiotic treatment by the physicians subsequent to the Gram staining result. The first telephone call contained the result of the Gram stain and the record of the current antibiotic therapy. The second telephone call took place 2 h after the first phone call and the antibiotic treatment was recorded again. Both phone calls were based on a standardized protocol and performed by medical doctors.

The final testing results allowed to evaluate, if the empiric antibiotic treatment before and after the communication of the Gram staining result was adequate. The final testing result was obtained after seven days and included the identification and the susceptibility of the pathogen. For identification Vitek MS (BioMerieux), for susceptibility testing Vitek 2 XL (BioMerieux), and for interpretation the EUCAST breakpoints (Version 8.0) were used.

In this study, adequate treatment was defined based on the following criteria: First, all Gram-negative rods, all candida, *Staphylococcus aureus*, *Streptococcus pneumonie*, *Streptococcus pyogenes*, *Streptococcus dysgalactiae*, *Enterococcus faecalis*, and *Enterococcus faecium* found in the culture needed to be covered. Second, the identified pathogen needed to be susceptible to at least one of the used antibiotics. This definition excluded facultative pathogens with a clinical case-to-case relevance like coagulase-negative staphylococci to prevent overestimation of the necessary antibiotic treatment.

Collected data included the time when the blood culture flagged positive, the time of the first phone call, the time of the second phone call, the result of the Gram stain, the antibiotic treatment at the time of the first phone call, the antibiotic treatment at the time of the second phone call, and the final result of the identification of the pathogen including its antibiotic susceptibility. The primary outcome was the average delay of the adjustment of an initial inadequate treatment to an adequate treatment. In addition, we describe the rate of adequate empirical antibiotic treatment before and after the communication of the Gram staining.

Results

Over a period of 3 months between June and August 2018, 336 patients had positive blood cultures for the first time. Of these, 152 had a positive blood culture outside of the conventional working hours. In total, 17 (10.5%) patients were excluded from analysis due to the following reasons: 7 patients had no pathogen in the first positive blood culture, 4 patients had an incomplete dataset, 2 patients were in a palliative care setting, 2 patients died before the Gram stain result was reported, and in 2 patients the pathogen could not be identified. A final number of 135 patients were included in the dataset. Of these, 67 patients had a pathogen that was likely necessary to be treated, 65 had a facultative pathogen, and 3 had a fungus.

In the following, the patients with a pathogen that was likely necessary to be treated are analyzed. Before the communication of the Gram staining out of 67 patients, 41 (61%) had an adequate and 26 (39%) an inadequate antibiotic treatment. After the communication, antibiotic treatment was adjusted in 15 (22%) of all 67 patients. This resulted in an increase of 8 percentage points to 46 (69%) patients with an adequate antibiotic treatment. Of the 26 patients with an inadequate empirical antibiotic therapy, 7 were adjusted and 19 were not adjusted. Of the 7 adjusted patients, 6 had an adequate and 1 an inadequate antibiotic therapy after the communication. Of the 41 patients with an adequate empirical antibiotic therapy, 8 were adjusted and 33 were not adjusted. Of the 8 adjusted patients, 7 had an adequate, and 1 an inadequate antibiotic therapy after the communication. There were 21 patients with an inadequate empirical antibiotic therapy after the communication. Six of them had no antibiotic treatment. Six had a non-guideline corresponding antibiotic treatment. Nine had a guideline-corresponding antibiotic treatment, but the pathogen was resistant to the chosen antibiotic treatment.

Of all 67 patients included in the analysis, the average delay between the blood culture flagging positive and the performing of the Gram stain was 9:59 h (IQR 6:05–13:49). The adequate antibiotic treatment in the subgroup of patients with an initial inadequate antibiotic treatment was delayed by 8:57 h (range 2:16–16:59).

Furthermore, there were 65 patients with a facultative pathogen in the blood culture. Because of the communication, an antibacterial treatment was started in 4 out of 10 patients. In total, out of the 65 patients, the antibiotic treatment was adjusted in 12 patients. In addition, we had 3 patients with fungus in the blood culture. Before the communication of the Gram staining, none of the patients had an antifungal treatment. Within the two-hour period after the communication, an antifungal treatment was started in 1 patient.

Discussion

This study evaluated the impact of the delayed communication of the Gram staining result made from blood cultures outside of conventional working hours. The communication of the Gram staining increased the rate of adequate antibiotic treatment by 8 percentage points. Nevertheless, the rate of the adequate antibiotic treatment after the communication was still only 69%. These findings are consistent with the current literature [4, 6]. The adequate antibiotic treatment with an initial inadequate antibiotic treatment was postponed on average by 8:57 h.

The patients in this study can be divided into four groups. The first group had adequate antibiotic therapy from the beginning. The second group received adequate antibiotic treatment as a consequence of the communication. Following the empirical guidelines, most of these patients should have received the antibiotic treatment when the blood culture was actually taken. The third group had a resistant pathogen to the antibiotic treatment that was in accordance with the empirical guidelines. This is unavoidable. In part, the high resistance rate can also be explained by the possible error rate of an antimicrobial susceptibility testing of piperacillin/tazobactam. The fourth group had no antibiotic treatment, and none was started. Either these patients did not need antibiotic treatment and should not have got blood culture diagnostics, or they were not optimally treated.

The benefit of the communication of the Gram stain microscopy result is limited by several factors. A positive blood culture can be the result of a contamination and therefore the information of the Gram stain can be misleading. In addition, the Gram stain result gives limited information about the antimicrobial susceptibility. Lastly, according to the guidelines, empirical antibiotic treatment can be started directly after the blood cultures are gained. Therefore, the delay of the communication of the Gram stain microscopy result may not be important. Nevertheless, the delay of processing positive blood cultures and of the antimicrobial susceptibility testing during the non-working hours could be a major disadvantage and could explain the reduction of mortality in other studies [4].

The main limitation of this study is the surrogate primary outcome, the average delay of the adjustment of an initial inadequate treatment to an adequate treatment. To observe mortality reduction directly was not feasible, because of the small effect sizes. All assumptions for the surrogate outcome were predefined and published before the study started and are consistent with the current literature. The assumption that a pathogen must be treated when found in a blood culture is based on the pathogenicity of its species and the clinical indication of blood culture diagnostics [8]. The definition of adequate antibiotic treatment is based on the final susceptibility testing result [9, 10]. The chosen 2-h period between the phone calls should be long enough to react to the communication of the Gram stain result and short enough to exclude most other changes in the antibiotic treatment. Another limitation is the assumption that the reaction to the communication of the Gram stain result is independent of the time of day. Lastly, the present study is a small single-center study. It is influenced by our in-house guidelines, standards, and conditions.

In conclusion, this study shows a benefit of the immediate communication of the microscopic Gram classification result. Nevertheless, this benefit seems to be partly the result of suboptimal adherence to the guidelines regarding empirical antibiotic treatment.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval No approval required according to the ethic committee of the University of Bonn.

Informed consent No approval required according to the ethic committee of the University of Bonn.

References

1. Rhodes A et al (2017) Surviving sepsis campaign: international guidelines for management of sepsis and Septic shock: 2016. Intensive Care Med 43(3):304–377
2. Goel G et al (2015) A method for early detection of antibiotic resistance in positive blood cultures: experience from an oncology centre in eastern India. Indian J Med Microbiol 33(Suppl):53–58
3. Jo SJ et al (2016) Direct identification and antimicrobial susceptibility testing of bacteria from positive blood culture bottles by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and the Vitek 2 system. Ann Lab Med 36(2):117–123
4. Barenfanger J et al (2008) Decreased mortality associated with prompt gram staining of blood cultures. Am J Clin Pathol 130(6): 870–876
5. Beekmann SE et al (2003) Effects of rapid detection of bloodstream infections on length of hospitalization and hospital charges. J Clin Microbiol 41(7):3119–3125
6. Cunney RJ et al (1997) The impact of blood culture reporting and clinical liaison on the empiric treatment of bacteraemia. J Clin Pathol 50(12):1010–1012
7. Moore JS, Koerner RJ (2015) In the era of the 24 h laboratory, does communicating gram stain results from blood cultures flagging positive outside of conventional working hours alter patient management? J Clin Pathol 68(11):938–941
8. Jindai K et al (2014) Is a single positive blood culture for Enterococcus species representative of infection or contamination? Eur J Clin Microbiol Infect Dis 33(11):1995–2003
9. Garnacho-Montero J et al (2015) Adequate antibiotic therapy prior to ICU admission in patients with severe sepsis and septic shock reduces hospital mortality. Crit Care 19:302
10. Riedel S et al (2006) Comparison of the BACTEC 9240 and BacT/alert blood culture systems for detection of bacterial contamination in platelet concentrates. J Clin Microbiol 44(6):2262–2264