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Original Article

Impact of interventions by an antimicrobial stewardship program team on appropriate antimicrobial therapy in patients with bacteremic urinary tract infection

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ABSTRACT

Background: Inappropriate antimicrobial therapy often leads to poor outcomes. This study aimed to evaluate the impact of an antimicrobial stewardship program (ASP) team on appropriate therapy, in patients with bacteremic urinary tract infection (UTI).
Patients and methods: We retrospectively reviewed the interventions by the ASP team in 807 patients with bacteremic UTI. Interventions were divided into 3 groups: group A (conventional report), group B (conventional report and written alert on the chart), and group C (conventional report and oral recommendation with/without written alert). The appropriateness of antimicrobial therapy was assessed at 2 time points, based on blood culture results.
Results: The ASP team estimated that 166 and 576 patients received inappropriate antimicrobial therapy based on the results of Gram staining, and final report, respectively. Appropriate therapy after intervention was administered to 53.2% of group A, 63.5% of group B, and 89.3% of group C patients, respectively. Mortality was significantly lower in patients of de-escalation than in those with no antimicrobial changes, without prolonged hospital stay.
Conclusion: This study provides one plausible benchmark for appropriate antimicrobial therapy by ASP, while observer bias and survivor treatment selection bias exist, and further studies including evaluation for severity are needed.

1. Introduction

It is important to initiate effective antimicrobial therapy in patients with bacteremia at the earliest convenience, because previous reports indicate a causal relationship between inadequate antimicrobial therapy and unsatisfactory outcome [1–3]. Paruk et al. reported that up to 55% of all patients with bloodstream infections (BSIs), received inadequate therapy during the empirical period (before microbiological report is available) [2]. Furthermore, several articles have reported that even after the final microbiological report, approximately 20% of patients with BSIs continue to receive inadequate antimicrobial treatment [4,5].

Conversely, inappropriate use of antimicrobials has been demonstrated to result in the emergence and transmission of multidrug-resistant bacteria [6–8]. De-escalation strategy aims at reducing the cost, minimizing medication related side effects and interactions, and lowering the risk of bacterial resistance [9,10].

With the increasing prevalence of multidrug-resistant bacteria, empirical use of broad-spectrum antibiotics in patients with sepsis becomes necessary, until microbiologic and susceptibility results become available. Once the reports are available, it is advisable to de-escalate from broad-spectrum to narrow-

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spectrum antimicrobials, and discontinue redundant antimicrobial coverage [7,11]. Several types of antimicrobial stewardship programs (ASP) including an interventional approach have reduced the inappropriate use of antibiotics, thus saving costs, without affecting patient mortality [7,9,12].

The aim of this study was to highlight the role of ASP team for appropriate use of antimicrobials in patients admitted to a university hospital with bacteremic urinary tract infection (UTI). The role of ASP in selecting antimicrobial therapy and desirable approach of intervention by ASP team were evaluated. Furthermore, outcomes were compared between patients with bacteremic UTI, in whom empiric antimicrobial coverage was de-escalated or adjusted based on culture and susceptibility data, and those in whom antibiotics were not de-escalated.

2. Patients and methods

2.1. Patient selection and study period

In this retrospective cohort study, medical records of all patients aged >18 years, who developed bacteremic UTI during hospitalization, at Nihon University Itabashi Hospital (NUIH) from April 1, 2008 to December 31, 2015 were reviewed. NUIH is a 1037-bed teaching hospital for Nihon University School of Medicine, and serves the catchment area to the north of Tokyo, Japan. All clinical records have been electronically maintained since January 1, 2014. Prior to this date, data of laboratory results have been electronically maintained, but written records were used for physicians' clinical documentation.

Bacteremic UTI episodes were identified from the clinical charts of all patients with significant levels of the pathogen isolated in blood cultures. UTI was confirmed by checking their records for evidence of an identical bacterium in the urine culture same as that in blood culture, with pyuria by dipstick or sedimentary urine analysis and/or clinical symptoms such as flank pain and fever, and without any evidence of other infection sites.

2.2. Processing of samples in the microbiology laboratory

For blood culture, we used culture bottles (BACTEC bottles 92F and 93F as 1 set, Becton Dickinson [BD] Diagnostic Systems, Franklin Lakes, NJ) and automated systems (BACTEC 9240 and 9120, BD Diagnostic Systems), with continuous agitation. Microorganisms were identified by Gram staining (neo-B, and M Wako, Wako Pure Chemical Industries, Osaka, Japan), using an uncentrifuged drop of blood, taken from the culture bottle, when bottles turned positive in the automated system. Identification and antimicrobial susceptibility tests were performed as appropriate for suspected microorganisms, using standard procedures recommended by the Clinical and Laboratory Standards Institute. For identification the bacterial species, several methods were used. These included assessment of morphologic appearance and colonies, and biochemical characteristics using manual procedures or commercial kits (API series, bioMérieux, l'Etoile, France; and N-ID test SP-18, Nissui Pharmaceutical, Tokyo, Japan), or an automated identification system (VITEK 2 system, bioMérieux, or RAISUS system, Nissui Pharmaceuticals Co., Ltd.). Antimicrobial susceptibility tests were performed by broth microdilution using National Committee for Clinical Laboratory Standards (NCCLS) breakpoints.

2.3. Reporting the results of microbiologic examination and interventions by the ASP team

For positive blood culture bottles, results of the Gram stain were reported on electronic medical charts, as well as to physicians in charge over phone, by the microbiology laboratory. The results of Gram stain were categorized as gram-positive cocci (*staphylococcus*, or *Streptococcus*), gram-positive rods, gram-negative cocci, gram-negative rods, fungi, and multiple microorganisms. Final reports were reported on the electronic medical charts after definitive identification of the pathogens and their susceptibilities.

In the NUIH, the ASP team comprises of certified infectious diseases specialists and residents who are studying to qualify as certified infectious diseases specialists. The ASP team undertook ward rounds for every episode of bacteremia in which the blood culture was positive, and Gram stain results had been reported, and recommended intervention every day, except non-consultation days, as indicated in our previous report [13]. The range of comments by the ASP team during ward rounds were: "continue the empiric antimicrobial," "adjust the empiric narrow spectrum to susceptible spectrum antimicrobial," "escalate of empiric narrow spectrum to broad spectrum antimicrobial," "de-escalate the empiric broad spectrum to narrow spectrum antimicrobial," "start an antimicrobial," or other comments.

Furthermore, the ASP team ward rounds were regularly conducted bi-weekly, for the patients with positive blood cultures, in whom antibiotic therapy had been administered. During these regular ward rounds, the ASP team checked the reports of identification and susceptibility, and intervened to recommend the appropriate antibiotic therapy, and to observe the clinical course.

While the ASP team basically recommended appropriate antibiotic therapy with a written report on the papery or electronic charts, the suggested interventions were of cumulative 3 different types, according to human resources and consultation days availabilities of the ASP team:

Group A (conventional report): the result of Gram staining was only communicated by the microbiology laboratory, and a report was produced after definitive identification and antimicrobial susceptibilities of the isolates.

Group B (written alert report on the papery or electronic clinical chart): In this group of patients, the procedure for group A was complemented with a written-alert report, to be included with the clinical chart. This report included therapeutic recommendations by the ASP team when the blood culture was positive, and results of Gram staining were available, or when the definitive identification and antimicrobial susceptibilities were determined.

Group C (oral alert report provided). This procedure included all information provided to group A and Group B, as well as a direct conversation with the physician in-charge concerning therapeutic recommendations by the ASP team, when the blood culture was positive and results of Gram staining were available, or when the definitive identification and antimicrobial susceptibilities were determined.

2.4. Antimicrobial therapy

Antibiotic therapy was assessed during the following time periods:

The empirical period, beginning from collection of the first blood culture sample, and ending when results of Gram stain for the positive blood culture bottles were available.

The "early" period, which started when the results of Gram staining were obtained, and ended when the final microbiological reports were received.

The "late" period, which started when the definitive susceptibility test results were available and ended with death or when antimicrobial therapy for the episode was completed.

Antibiotic de-escalation was defined as changing the empiric or early period antibiotic regimen, to a culture-specific agent with a narrower spectrum, compared to that of the original empiric or

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