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ORIGINAL ARTICLE

Antibiotic utilization pattern in a general medical ward of a tertiary medical center in Saudi Arabia

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ABSTRACT

To assess the pattern of antibiotic utilization and outcome of patients with bacteremia in a General Medical Ward, all positive blood cultures (BC) over a 12-month period from January 1994 to December 1995 were retrospectively reviewed. Fifty-two positive BC were recorded in 43 patients (63% males, 37% females; mean age 65.9 $\pm$ 16.6). 72% of the patients received antibiotics before or soon after obtaining the BC, and ceftriaxone was the most frequently-prescribed antibiotic (41.93%), either alone or in combination with other antibiotics. The bacteremia was due to gram-positive cocci in 60.46% of cases, gram-negative rods in 30.23%, and gram-positive rods in 9.30%. Positive BC due to contamination were not included. The most common gram-positive cocci were *Staphylococcus epidermidis*, followed by *S. aureus*, while the most common gram-negative bacilli were *Brucella* species, *Proteus mirabilis*, and *Klebsiella* sp. The suspected sources of the bacteremia were respiratory (21.2%), urinary (19.2%), or skin (19.2%). A subsequent change in the antibiotics regimen was done in 69.76% cases after BC results became available with no apparent effect on the outcome. Adding vancomycin and clindamycin was the most frequent change done (19.4% for each equally). Complications developed in 69.76% of patients, with 88.66% of them suffering from sepsis/shock. 69.23% of the patients improved and 30.77% expired; death was related to infection in 87.5% of cases. In conclusion, most bacteremia in the medical ward of the hospital were due to gram-positive cocci, which should be considered in antibiotic selection prior to BC. Risk factors for acquiring Brucellosis should always be obtained.

Key words: Antibiotic, medical, Riyadh, Saudi Arabia, utilization

INTRODUCTION

In the developing nations, the cost of drugs is a major concern to medical health care professionals and patients. It has been seen that antibiotic expenditures account for nearly 50% of a hospital's total drug budget.[1] Extensive mistreatment of antimicrobial drugs has been reported in the past few years, and nearly half of all antibiotic drug prescriptions have been found to be poorly selected. This is especially true for the general wards in tertiary medical centers (TMC) where errors in prescription, administration, and delivery are common. In such scenarios, the possibility of drug interactions and adverse drug reactions are high, as large numbers of medications are prescribed. Additionally, inappropriate and unreasonable utilization of antimicrobials can cause microbial resistance to the commonly-prescribed antimicrobials.[2] This, in turn, can contribute to the use of newer, more costly antibiotics to fight the crisis of microbial resistance.[1] This is an issue of great concern to a developing country like Saudi Arabia.

Analysis of drug prescription practices is of special interest with respect to increasing costs of health service. The prescribing pattern can be evaluated in a retrospect manner through analysis of clinical records in a medical care center.[3] The study of prescription pattern is generally a part of a medical audit that looks for appraisal, and, if required, modification, in prescription pattern, to obtain rational and cost-effective medical care.[4]

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Review of the antimicrobial agent utilization in the TMC and information about the various strains of microorganisms and their sensitivity patterns are helpful in developing infection control plans in the TMC.[3] Development of resistant microorganisms due to inappropriate use of antibiotics can result in the spread of these microorganisms to other patients admitted in the same ward.[2] Hence, prevention of inappropriate antibiotics use is vital for infection control plans in the TMC.

With the purpose of assessing the pattern of antibiotic utilization and outcome of patients with bacteremia, this report shows the results of a retrospective analysis of the pattern of antibiotics use over a 1-year period (January 1995 to December 1995) in the general medical ward of TMC in Saudi Arabia.

MATERIALS AND METHODS

Study design

We retrospectively monitored all patients admitted in a general medical ward of a TMC in Saudi Arabia, over a period of 12 months between January 1995 and December 1995.

Setting

A general medical ward of a Tertiary Medical Center in Saudi Arabia.

Patient data

For all patients, clinical and laboratory data which were recorded by trained physicians and nurses during the period of hospitalization were utilized. The patients were considered to have infection if they had at least one positive blood culture (BC) for organisms known to cause bacteremia. Any nosocomial infection was defined by Standard Centre for Disease Control and Prevention.

Blood culture

10 ml of venous blood from the patients was obtained aseptically. The collected blood was sent to laboratory for identifying the organism responsible for bacteremia. Enriched and selective media including blood, MacConkey and chocolate agar plates were inoculated at 37ºC, and examined for growth at 24–48 h. Isolates, if any, were identified by standard microbiologic procedures, including Gram staining, colony characteristics, and biochemical properties such as catalase, mannitol salt agar, DNAse agar, and hemolysis on blood agar plates, for Gram-positive isolates; and triple sugar iron (TSI), lysine iron agar (LIA), citrate, urease, and oxidase for Gram-negative bacilli.[5] Antibiotic susceptibility was performed by the Kerby-Bauer disc diffusion method including standard oxacillin disc susceptibility as well as optochin and bacitracin.[5] The isolated microorganisms were frozen in glycerol broth at −70ºC for further identification.

RESULTS

A total of 43 patients who were admitted to the hospital were affected by infection. Of these 43 patients, 27 (63%) were males and 16 (37%) were females. The mean age of patients was 65.9 $\pm$ 16.6. A total of 52 positive BC were collected from 43 patients. From all patients admitted, 31 (72%) had received antibiotics before or soon after obtaining the BC, but before the arrival of results. It was observed that ceftriaxone was the most frequently-prescribed antibiotic before the results were obtained. Of the 31 patients receiving antibiotics before culture report, 13 patients (41.93%) had received ceftriaxone, either alone or in combination with other antibiotics.

Upon examining BC results, it was clear that the bacteremia was caused by gram-positive cocci in 26 patients (60.46%), gram-negative rods in 13 patients (30.23%), and gram-positive rods in 4 patients (9.30%). Positive BC from contamination were not included for analysis, including contamination from health care workers or as a result of other procedures. Various gram-positive cocci were identified, including *Staphylococcus epidermis*, *Staphylococcus aureus*, Coagulase-negative Staphylococcus, *Enterococci*, and *Streptococcus pyogenes*. The most common gram-positive cocci were *S. epidermidis*, followed by *S. aureus*. The gram-negative bacilli identified were *Brucella* species, *Proteus mirabilis*, and *Klebsiella* sp. The suspected source of the bacteremia was identified in 26 patients, including respiratory (21.2%), urinary (19.2%), or skin (19.2%).

From the BC results, subsequent changes in the antibiotic treatment were ordered in 30 patients (69.76%), only for those who failed to have a positive outcome from initial antibiotic therapy. Most of the patients received an add-on therapy of vancomycin or clindamycin.

A total of 30 patients (69.76%) experienced complications due to their infection. Of these, 26 patients (88.66%) developed serious sepsis or septic shock. Of the patients who had septic shock or serious sepsis, 18 (69.23%) improved and 8 (30.77%) had fatal outcomes. Death was associated with severe infection in 7 cases (87.5%).

DISCUSSION

Throughout various studies completed worldwide, it has been seen that monitoring of systems and intervention are useful in improving the quality of the health care system.[4] This is especially relevant for the appraisal of antibiotics utilization culture in health institutions. Prescribers worldwide are increasingly running out of antibiotic options as a result of the sinister pace with which antibiotic resistance develops in bacterial infections.[6-8] The high rate of antibiotic use combined with the high percentage of critically ill patients has made the intensive care units (ICU) a major source of antibiotic resistant nosocomial infections[9,10] which spread to other parts of the hospital and to the wider community. In a 2010 study investigating the factors driving the development of third-generation cephalosporins resistance in *Escherichia coli* and methicillin-resistant *Staphylococcus aureus* (MRSA), Borg *et al.,* found a positive correlation between the level of antibiotic administration and resistance development.[11] From their findings, they recommended a judicious use of antibiotic agents especially in the developing countries. 50% of prescribed antibiotic use in antibacterial prophylaxis and treatment were said to be unnecessary.[12,13] An instance was presented in a 2006 Cochrane report highlighting how no additional benefit was obtained by prolonging antibiotic prophylaxis beyond 24 h in preventing post-surgery intracranial ventricular shunt infections.[14]

In the present study, a survey of drug utilization pattern in a tertiary care center in Saudi Arabia was conducted. To the authors' best knowledge, this is the first study which assessed the pattern of antibiotic utilization and outcome in patients with bacteremia in a TMC in Saudi Arabia.

In this study, a high proportion of patients were observed to receive antibiotics treatment prior to the availability of the results from BC tests. This prescribing behavior is possibly related to the attitudes of health care professionals and patients toward antibiotic use in patient management. Admittedly, this may be crucial for arresting or preventing the spread of infection in severe infection cases. In such cases, the experience of the prescriber is called upon in selecting the appropriate antibiotic treatment with an antibacterial profile covering the suspected infectious agents. It is, however, important that such use be limited to an initial intervention therapy soon replaced by selections based on antibiotic sensitivity result. In any case, the possibility of selecting antibiotic-resistant strains is increased in antibiotic use not guided by microbiological culture results. This in turn makes future antibiotic treatment increasingly difficult. In addition, the adverse drug reactions associated with such antibiotics are likely to further complicate treatment plan.

In the present study, the most commonly prescribed drug for this indication was the third-generation cephalosporin, ceftriaxone. The antibacterial activity of ceftriaxone covers *Streptococci, Staphylococci, Citrobacters, Gonococci, Shigella, and Clostridia* infections, which are normally susceptible to ceftriaxone treatment.[5] Thus, its administration in *Brucella* infections rather than eliminate the infection, unnecessarily exposes the patients to adverse drug effects associated with its use. It also alters the body's microbial flora and supplies an antibiotic selection pressure that selects resistant strains of the infectious agents. This scenario highlights the role of culture and sensitivity tests before determining which antibiotic, including a cephalosporin, will best control an infection caused by specific strains of bacteria.

Although most of the patients had infection from gram-positive organisms, approximately 30% of patients had infection due to gram-negative organisms, such as *Brucella*. Change in treatment was accomplished in 30 patients who did not respond to the initial treatment, and such change often involved addition of vancomycin or clinidamycin to the antibiotic regimen. While the need for antibiotic change may be as a result of demonstrated greater antibacterial effects of the new medications, it is also likely to be an indication of the involvement of antibiotic resistance in the patients group. This is somewhat similar to the outcome of a 2009 survey, employing physicians from 24 European countries, where third-generation cephalosporin resistance was said to be the most frequently observed after MRSA.[9,15]

A physician will not always be able to determine the identity of the microbial organism involved in infection before BC results are available. In this case, a crucial factor influencing the decision of treatment options is the prescriber's familiarity with antibacterial infections and susceptibility pattern in the local community. As observed in the present study, in most of the investigated cases, the initial antibiotic treatment was characterized by resistant gram-positive strains as well as antibiotic resistant gram-negative organisms. In such a situation, the ideal treatment option would be the administration of antibiotic agents capable of eradicating both types of infection. However, such ideal antibiotic agents are generally difficult to come by especially with the continual absence of new mechanisms of antibiotic action in pharmaceutical companies' discovery pipeline. There is, therefore, an urgent need for a review of antibiotic utilization policies and use should be strictly guided by microbial culture and sensitivity tests as much as possible.

It is also possible that the selection of antibiotics was based on the sources of infection, which in most of the investigated cases were respiratory, skin, and the lower urinary tract. However, selection merely based on this property often further complicates the clinical course of treatment. Approximately 70% of the studied cases had complications due to infection, of which seven fatalities were recorded. This further highlights the reason why proper antibiotic selection is crucial when commencing antibiotic treatment prior to the availability of microbiological culture and antibiotic sensitivity test results.

The current study is however not without some limitations. In the first instance, a the study employed a small number in a single TMC for which reason caution may be necessary in extending the conclusions to larger number of patients. Also, we only considered drug utilization pattern over a 1-year period which may be different from the pattern obtained over longer period. The study was retrospective and data on the grade of severity of illness of admitted patients was not available in the case records. For this reason, it was not possible to correlate the drug utilization patterns with the severity of patients' illness. However, the study provides, at a glance, the pattern of antibiotic agent utilization in tertiary health institutions within the considered 1-year period, the relationship between utilization and the observed resistance distribution pattern. While the need for the commencement of antibiotic treatment in serious infections ahead of microbiological test results was recognized, this study also highlights the risk associated with such use. This necessary prescription in the absence of culture results should ideally be limited to a single initial dose after which subsequent treatment should be based on microbial culture and sensitivity test results. This ensures the use of narrow-spectrum antibiotic agents, thus reducing the risk of antibiotic resistance development.[16] It is also recommended that antibiotic management guidelines should, as much as possible, limit the pre-culture use of antibiotic agents with broad-spectrum antibacterial effects (e.g., the third-generation cephalosporins) to a single starting dose or 24 h depending on when microbiological results are available. This change of attitude toward antibiotic utilization has the potential to reduce the risk of selection of multi-drug resistant strains and decrease the cost of drug treatment, a significant proportion of which goes to antibiotic use.[12]

CONCLUSIONS

Our study concluded that most bacteremia in the medical ward of the hospital were due to gram-positive cocci, which should be considered in antibiotic selection prior to BC, and risk factors for acquiring Brucellosis should always be obtained. This would not only help to control drug expenditures, but also minimize the potential health hazards from unnecessary antibiotics consumption. Also, strict protocols for practitioners need to be designed to avoid the use of unnecessary antimicrobial drugs.

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