Dynamics of Antibiotic Usage in the Intensive Care Unit at the University Hospital of the West Indies

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ABSTRACT

Objective: To determine antibiotic usage patterns in the Intensive Care Unit (ICU) at the University Hospital of the West Indies (UHWI).

Method: A cross-sectional, analytical study of consecutive patients admitted to the ICU was conducted between July and December 2007. Exclusion criteria were HIV-positive patients, patients < 12 years and those discharged or who died within 48 hours of admission. Data were collected from medical records, stored and analysed using the SPSS Version 12.

Results: Of the 150 eligible patients, 109 had complete data (73%). Mean age was 50.8 ± 20.7 years, with mean APACHE II score of 15.6 ± 6.7. Forty-five patients (41.3%) received prophylactic antibiotics, most commonly ceftriaxone (31.7%) and metronidazole (19.0%). Appropriate discontinuation within 24 hours occurred in only 11.1%. Two-thirds of patients (67.9%) were treated with empiric antibiotics, most commonly piperacillin/tazobactam (32.1%), ceftazidime (27.5%) or metronidazole (27.5%). Reasons for empiric choice were primarily coverage of organisms based on presumed source of sepsis (45.6%), and broad spectrum, high-powered coverage (23.5%). Courses ranged from 1 – 42 days and were adequate based on subsequent cultures in 71% of cases. Culture reports took between 2 – 8 days with a mean of 3.7 days to become available. De-escalation was practised in only 2 of 26 (7.7%) cases and intravenous to oral switch therapy in only 3.3%. Thirty-two (29.4%) patients died, with sepsis being a cause in 12 (37.5%).

Conclusions: Improved attention to discontinuation of prophylactic antibiotics, appropriate duration of antibiotic courses and de-escalation are essential if the antibiotic practices in the ICU at the UHWI are to compare favourably with international recommendations.

Keywords: Antibiotic use, de-escalation, Intensive care

Dinámica del uso de Antibióticos en la Unidad de Cuidados Intensivos del Hospital Universitario de West Indies

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RESUMEN

Objetivo: Determinar los patrones de uso de antibióticos en la Unidad de Cuidados Intensivos (UCI) en el Hospital Universitario de West Indies.

Método: Se llevó a cabo un estudio analítico transversal de un número de pacientes consecutivos ingresados a la UCI entre julio y diciembre de 2007. Los criterios de exclusión fueron los siguientes: pacientes positivos al VIH, pacientes < 12 años, y pacientes dados de alta o fallecidos dentro de las 48 horas de su ingreso. Los datos fueron tomados de las historias clínicas, y luego almacenados y analizados usando la versión doce de SPSS.

Resultados: De los 150 pacientes elegibles, 109 completaron los datos (73%). La edad promedio fue 50.8 ± 20.7 años, con una puntuación APACHE II media de 15.6 ± 6.7. Cuarenta y cinco pacientes (41.3%) recibieron antibióticos profilácticos, por lo general ceftriaxona (31.7%) y metronidazol (19.0%). Una descontinuación adecuada dentro de las 24 horas se produjo en sólo 11.1%. Dos tercios

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de los pacientes (67.9%) recibieron tratamiento antibiótico empírico, por lo general con piperacillina-tazobactam (32.1%), ceftazidima (27.5%) o metronidazol (27.5%). Las razones para la opción empírica fueron principalmente la cobertura de organismos sobre la base de fuentes de sepsis presuntiva (45.6%), y el espectro ancho, cobertura de alta potencia (23.5%). Los cursos fluctuaron de 1 – 42 días y fueron adecuados a juzgar por los cultivos subsiguientes en 71% de los casos. Los reportes de cultivos tomaron entre 2 – 8 días con un promedio de 3.7 días para hallarse disponibles. El desescalamiento fue practicado en sólo 2 de 26 (7.7%) de los casos y cambio de terapia intravenosa a oral en sólo 3.3%. Treinta y dos (29.4%) pacientes murieron, siendo la sepsis la causa en 12 (37.5%).
Conclusiones: *Una mayor atención en cuanto a descontinuar el uso de antibióticos profilácticos, una duración apropiada de cursos antibióticos, y el desescalamiento, son esenciales si se quiere que las prácticas antibióticas en las UCI en el HUWI puedan compararse favorablemente con las recomendaciones que se hacen a nivel internacional.*

Palabras claves: Uso de antibióticos, desescalamiento, cuidado intensivo

INTRODUCTION

Although intensive care units (ICUs) account for fewer than 10% of total hospital beds, over 20% of nosocomial infections are acquired there (1). This is related to an immuno-compromised patient population and the presence of invasive lines and tubes which breach normal barriers to infection (skin and mucous membranes). Intensive Care Unit acquired infections account for substantial morbidity, mortality and expense (2).

Antibiotics are important in the prevention and treatment of nosocomial infections. Prophylactic antibiotics are used where there is a high risk of developing an infection and should be discontinued within 24 hours. Empiric antibiotics are started when the patient has features of an infection, including pyrexia and leucocytosis but examination findings and laboratory data are not yet available. The current recommendation, which has been shown to reduce mortality rates in hospitalized patients with serious infections, is prompt initiation of broad-spectrum, high powered antibiotics to ensure coverage, then de-escalation or streamlining therapy when a pathogen is identified and switching from intravenous to oral therapy when clinically indicated (3, 4).

Inappropriate antibiotic use is associated with numerous problems including development of antibiotic resistance (5) which is an important determinant of mortality for patients in the ICU (4). Despite concerns surrounding the use of antimicrobials, there are limited controlled data to guide the intensivist in making decisions concerning indications for therapy, choice of antibiotics and duration of course in the ICU. At the University Hospital of the West Indies (UHWI), ICU space is limited and in high demand (6). Strategies to reduce the length of ICU stay and attendant costs, such as the prescription and administration of timely, appropriate and adequate antibiotics, will be invaluable. Therefore, the aim of this study was to determine antibiotic usage patterns in the ICU at the UHWI and to compare the practices with international standards to identify areas for improvement.

SUBJECTS AND METHODS

Approval for this study was obtained from The University of the West Indies/ University Hospital of the West Indies Ethics Committee. The UHWI, Kingston, Jamaica, has two multi-disciplinary, open ICUs with a total of 16 beds. A cross-sectional, analytical study was done on patients admitted to the UHWI ICUs between July 1, 2007 and December 31, 2007. Patients excluded from the study were those who were HIV positive, less than 12 years old, discharged or who died within 48 hours of admission or whose ICU stay exceeded 60 days.

Data were collected from the medical records of all eligible patients and included age, gender, APACHE II score on admission, referring specialty, pre-existing antibiotic use, patient outcome and length of ICU stay. All culture reports and antibiotics commenced were recorded, with reasons for commencing and for choice and length of course. Data were analysed using SPSS Version 12.0.

RESULTS

Of the 150 patients eligible, complete information on 109 was found (73%). The study included 56 females (51.4%) and 53 males (48.6%). Their mean age was 50.8 ± 20.7 years and their illness severity was represented by a mean APACHE II score of 15.6 ± 6.7. Over three-quarters (81.7%) were emergency admissions. A total of 73 patients were surgical (67%), 32 were medical (29.4%) and 4 were obstetrical/gynaecological (3.7%). Sepsis was the reason for admission in 28 patients (25.7%), and in 16 of these (14.7%) perforated or leaking abdominal viscera were the initial source of infection. Other reasons for admission included postoperative neurosurgical patients (17.4%), respiratory failure (11.1%) and trauma (9.2%). Average length of ICU stay was 11 ± 11.5 days with a range of 2 to 58 days and a median of six days. Thirty-two (29.4%) patients died with sepsis being the main cause in 12 (37.5%). Six of the latter had abdominal sepsis (50%), two pneumonia (17%) and one patient each had flame burns, multiple trauma, massive gastrointestinal bleed-

ing and decompensated sickle cell disease (HbSS). Average time from admission to death was 9 ± 7.7 days.

Pre-admission Antibiotics
Only 20 patients (18.3%) were being treated with antibiotics on admission. Common pre-admission antibiotics were cefuroxime (15%) or a combination of amoxicillin/clavulanic acid and ceftazidime (15%). Reasons for commencing preadmission antibiotics included presumed lower respiratory tract infection (40%), postoperative infections (20%) and septic shock (15%).

Prophylactic Antibiotic Usage
Forty-one per cent of patients (n = 45) received prophylactic antibiotics. The most frequently administered were ceftriaxone (31.7%) and metronidazole (19.0%) [Fig. 1]. The
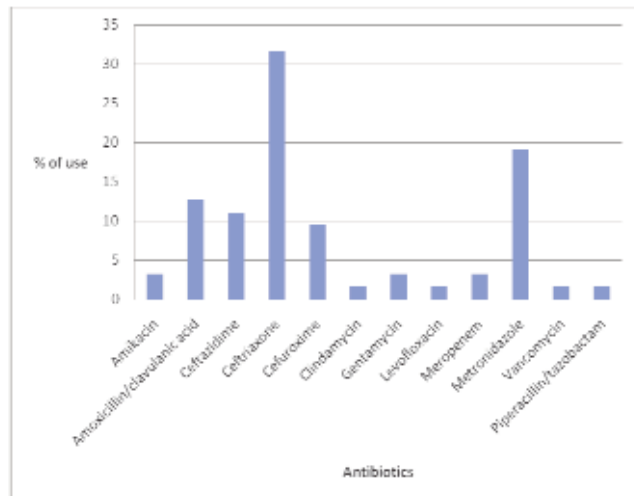

Fig. 1:   Prophylactic antibiotic usage in the intensive care unit

duration of the courses of prophylactic antibiotics ranged from 1–15 days, with a mode of two days. Appropriate use, with discontinuation within 24 hours, was practised in only 11.1% of cases. The most common reason for the choice of prophylactic antibiotics was "coverage based on the surgical site and/or possible organisms" (58.7%) followed by "based on experience" (23.8%).

Empiric Antibiotic Usage
Two-thirds (67.9%) of ICU patients were treated with empiric antibiotics. The most common was piperacillin/tazobactam (32.1%), followed by ceftazidime and metronidazole at 27.5% each (Fig. 2). The most frequent reason for starting empiric antibiotics was the presence of clinical correlates (50%).

Empiric antibiotics were chosen most frequently to ensure coverage of the likely organism based on presumed source of infection (45.6%). Meropenem and piperacillin/tazobactam were chosen for their high powered, broad spectrum profiles (23.5%). Physician experience was the reason
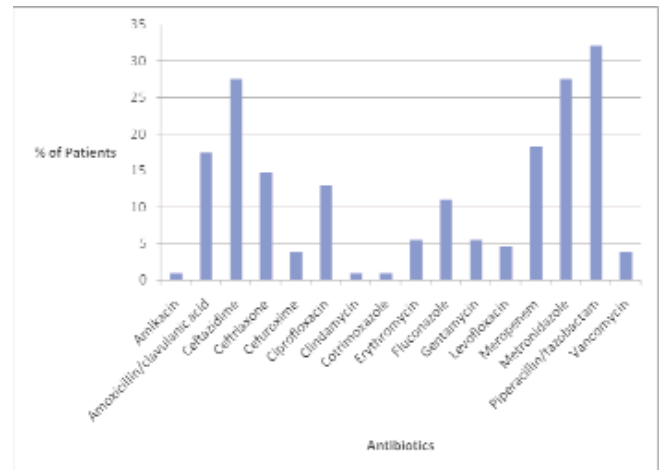

Fig. 2:   Empiric antibiotic usage in the intensive care unit

for choice in 12% of cases and only 1% was based on surveillance reports alone (Fig. 3). The duration of treatment
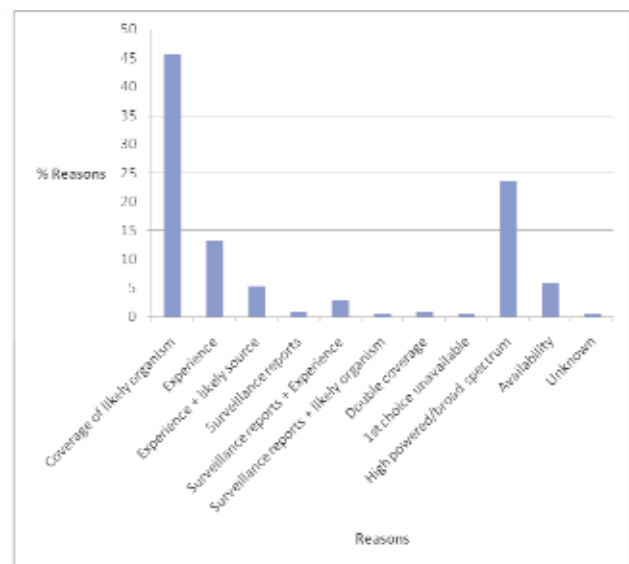

Fig. 3:   Reasons for choice of empiric antibiotic therapy

ranged between 1 to 42 days, with a mode of two days. The most common reason for discontinuing antibiotics was completion of course (43.4%), followed by demise of the patient (26.5%). Empiric antibiotics were not discontinued because therapy was appropriate in 38% of cases, and hence became culture-directed. In 34% of cases, no reason could be found for continuing empiric therapy (Fig. 4).

Empiric antibiotic choice was deemed adequate if the organism cultured was sensitive to that antibiotic and the overall adequacy rate was 71%. Piperacillin/tazobactam was adequate in 80% of cases and meropenem in 83.3% (Fig. 5). De-escalation was only possible in 26 cases and was practised in two (7.7%). Of the 30 patients who received
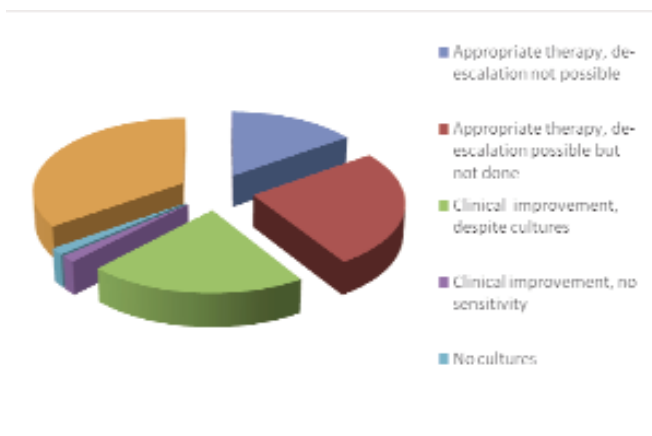
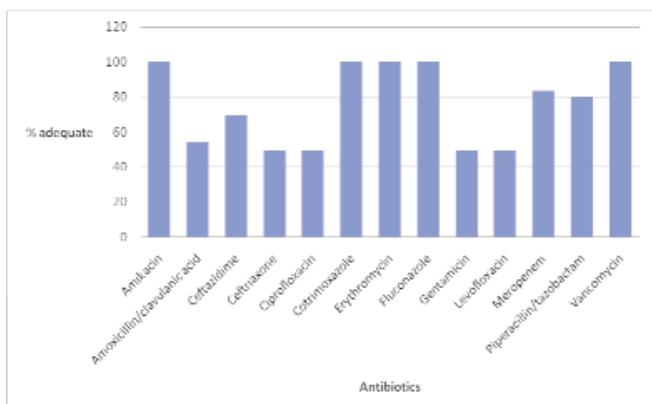Fig. 4:   Reasons for not discontinuing empiric antibiotic therapy

Fig. 6:   Culture-directed antibiotic usage

Fig. 5:   Adequacy of empiric antibiotic therapy

obtained the reports, ranged from zero to three days, with a mean of 0.6 days, median of zero days and mode of zero days.

ciprofloxacin, only one was switched from intravenous to oral administration after two days of intravenous use, a 3.3% switch rate. However, in another 3 of these 30 patients (10%), the oral preparation of ciprofloxacin was used initially, without previous intravenous administration. Other antibiotics given orally were cotrimoxazole, fluconazole, levofloxacin, and metronidazole, but each was only used in one patient respectively.

Culture-directed Antibiotics
The most commonly prescribed culture-directed antibiotic was ciprofloxacin (13.8%), followed by ceftazidime (8%) and meropenem (5%) [Fig. 6]. Ceftriaxone and cefuroxime were never prescribed guided by cultures. The length of culture-directed antibiotic courses ranged from less than one day to 20 days, with the most common duration being 10 days.

The time to obtaining culture reports ranged between two to eight days with a mean of 3.7 days, median of three days and mode of two days. The number of days which elapsed before antibiotics became culture-directed, having
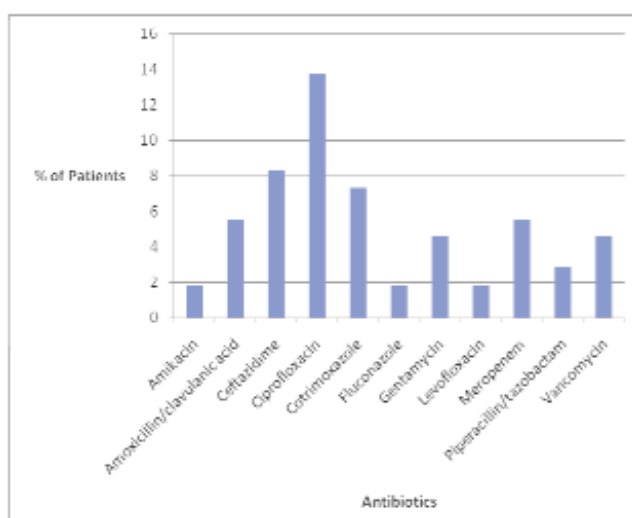
DISCUSSION
Studies have identified prior administration of antibiotics as a potential risk factor for inadequate antimicrobial treatment of infections (3, 7). This practice appears to predispose to colonization with bacteria that are often resistant to the previously prescribed classes of antibiotics (8). The majority of patients (81.7%) admitted to the ICU were not receiving antibiotics prior to admission. This reflects the high number of admissions not due to sepsis initially (74.3%). However, the study did not consider recently completed courses of antibiotics.

Improper use of prophylactic antibiotics, as occurred in 88.9%, adds to overall costs and may contribute to the selection of resistant organisms (9–13). The reason for prolonged use of prophylactic antibiotics was often the insistence of the admitting surgeon. To be effective, the antibiotic selected should have activity against those organisms most likely to contaminate the tissue (9). In many instances, no data was available to assist choices, and hence, it was not uncommon to see experience being the basis for the selection.

It should be clear that empiric antibiotic therapy should be used only as an initial approach. Unfortunately, many complicated patients are frequently continued on the initial empiric antibiotic regimen without adjustments (9). This practice results either from delays in provision of sensitivity reports from the laboratory or from the clinician's own failure to seek out such information. In this study, piperacillin/ tazobactam was used most frequently and was adequate in 80% of the cases. Ceftazidime was the next most commonly used (27.5%) but provided adequate coverage in only 69.2% of patients. Meropenem was administered to 18.3% of patients and was adequate in 83.3% of cases. Several epide-

miologic studies have suggested that inadequate antibiotic treatment of ventilator-associated pneumonia is an important determinant of hospital mortality (3, 14–15). Luna *et al* (16) found that subsequent changes in antimicrobial therapy based on culture results for patients who initially received inadequate treatment did not reduce their increased risk of hospital mortality. Ceftazidime cannot therefore be considered appropriate empiric therapy in light of the documented impact of inadequate initial treatment.

Empiric antibiotic therapy was initiated for legitimate reasons (to ensure coverage based on presumed source or for broad-spectrum, high powered profiles) but was appropriate in only 71% of cases. Surveillance reports alone constituted only 1.0% of reasons and this highlights the lack of up-to-date surveillance reports to help guide choices. Many studies have shown that local patterns of resistance must be known for appropriate empiric choices to be made (4, 17–21). The study of Tennant *et al* at the UHWI, ICU, looked at resistance patterns of common organisms and suggested empiric antibiotic regimes (22). At that time, antibiotics such as piperacillin/tazobactam were not commonly used, and amoxicillin/clavulanic acid was the recommended empiric antibiotic for gram positive organisms on the initial gram stain. This study showed that amoxicillin/clavulanic acid is now adequate as empiric therapy in only 54.5% of cases. Nicholson *et al* looked at the distribution of ICU organisms and their resistance patterns between 2002 and 2004 (23). Overall, common organisms were gram negative and included *Pseudomonas aeruginosa, Acinetobacter spp* and *Stenotrophomonas maltophilia.* These organisms demonstrated multiresistance. *Pseudomonas aeruginosa* was 63% resistant to ciprofloxacin, 42% resistant to gentamicin and 35% resistant to ceftazidime. *Acinetobacter spp* was even more resistant, with 97% resistance to ciprofloxacin, 87% to ceftazidime, 38% to meropenem and 30% to amikacin.

The ideal length of antimicrobial therapy remains very controversial and there are few published recommendations. The American Thoracic Society and Infectious Diseases suggest a 7–8 day course for non-pseudomonal nosocomial pneumonia where initial treatment was appropriate (17). The duration of therapy must therefore be considered for each patient according to the site of infection, the micro-organism involved and the response to therapy. Development of resistance is possible with inappropriate duration of courses (17). In this study, empiric antibiotic therapy ranged from 1 to 42 days. It is possible that the very short courses represented a change in antibiotic when culture reports became available. The very long courses are more difficult to explain, except in the case of treatment of *Stenotrophomonas maltophilia* where a 21-day course is recommended by the Microbiology Department. Unfortunately, many of the prolonged courses may represent a lack of vigilance on the part of the ICU doctors.

The practice of intravenous to oral switch therapy is a relatively new one in ICU. The antibiotics administered oral-ly are those with documented high bioavailability and have few gastrointestinal side effects (24). The oral switch rate was 3.3% and only 10% of all patients receiving ciprofloxacin were given the oral preparation. One possible cause for the reluctance to switch to oral therapy may be the belief that all ICU patients have questionable absorption of oral medications. Once patients are haemodynamically stable and do not demonstrate impaired absorption, oral switch can be considered. Intravenous to oral switch has several important advantages, including reducing drug cost and eliminating line phlebitis and sepsis with their cost implications (25).

In this study, de-escalation was practised in only 7.7% of possible cases. The implications of this include the risk of development of resistance to these antibiotics, and the unnecessary costs of using more expensive antibiotics. It takes a minimum of 48 hours to obtain preliminary blood and sputum culture reports. If positive, it can take up to five days for a full sensitivity report and identification of the organism. Urine culture reports, if negative, are available within 24 hours but if positive, in two to three days. Therefore the mean time to obtain culture reports of 3.7 days was not unreasonable. However, at no time should there be a delay in adjusting therapy once the culture reports become available. In this study, this ranged from 0 – 3 days, suggesting the need for improvement. 'Stat' antibiograms including plating of the original specimen and applying antibiotic discs, even before isolation/identification of the organism would facilitate a much faster turn-around of reports.

Limitations of this study are primarily related to its retrospective nature. It also did not specifically address microbiological confirmation of presumed pathogens and hence the potential role of multiple-resistant isolates on antibiotic choice and usage. This study did not look at outcome and is unable to determine whether patients would have improved, with or without antibiotics in those cases where no organisms were isolated or whether viral, fungal or parasitic infections were involved. These are aspects of antibiotic usage that should be addressed in future prospective studies.

CONCLUSION
This study has highlighted the need for more stringent controls of antibiotic use in the ICUs at the UHWI if it is to meet international recommendations. Recommendations include the discontinuation of all prophylactic antibiotics within 24 hours and the ICU clinician should encourage admitting physicians to adopt this practice. Prompt collection of culture reports with early institution of a culture-directed antibiotic regime, including de-escalation when possible is imperative.

The latter will require early and regular consultation with the Microbiology department to determine common isolates and their antibiograms and to facilitate the development of appropriate empiric protocols. An Antibiotic Control Policy needs to be established and implemented and a multi-disciplinary team approach developed to antibiotic usage.

Attention needs to be paid to length of courses of antibiotics and each course should have a predetermined, documented stop date which can then be reviewed. Training programmes in appropriate antibiotic use should be incorporated in the teaching of residents and for continuing medical education of personnel at all levels.

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