

Antibiotic Administration in the Intensive Care Units (ICUs) of a Tertiary Care Hospital of Tirana, Albania

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In intensive care units (ICUs) patient conditions, signs of infection and inflammation are similar, making the diagnosis of bacterial infections difficult. As a general rule to prevent or cure the disease caused by an unknown agent, antibiotics may therefore be overused, contributing to the development of antibiotic-resistant bacteria. The aim of this study was to determine the pattern of antibiotics administered in the ICUs and to compare these practices with international standards to identify possible improvement. The study was conducted in October 2015 at four ICUs at the University Hospital Center ‘Mother Teresa’ in Tirana, Albania with an overall capacity of 50 beds. Data were collected using a ward form and a patient form referring to the Global Point Prevalence Survey (Global PPS) methodology. The patients form was fulfilled for all inpatients under antibiotic treatment at 8 a.m on the day of the survey. A total of 17 types of antibiotics were used, which an average of 1.4 antibiotics per patient. In our study, 8 patients (16.3%) out of 49 patients did not receive any antibiotic, whereas the remaining 41 (83.7%) patients received one or more antibiotic. The reason to prescribe the antibiotic therapy was determined in 46 out of 49 cases (94%) and most frequently empiric antibiotics were chosen to ensure coverage against the most-likely microorganism only on the base of the presumed source of infection. The most commonly prescribed antibiotic was ceftriaxone (10.2%) followed by ciprofloxacin (8.2%), and meropenem (4.1%). Due to the large number of healthcare workers and the possible transmission of pathogenic bacteria from patient to patient, ICUs are high-risk wards with for the spread of antibiotic-resistance bacteria. Prompt collection of culture reports and early set-up of a culture directed antibiotic regime, including a possible de-escalation when possible is imperative. This will require early and regular consultation with the Microbiology Department to identify common isolates, their antibiotic sensitivity by antibiograms and the appropriate treatment protocol. These data suggest that an Antibiotic Control Policy needs to be established in the ICUs and a multidisciplinary approach should be developed for a correct and specific antibiotic administration.

Keywords: intensive care unit, antibiotic therapy, guidelines

1. Introduction

Even though intensive care units (ICUs) account for fewer than 10 percent of total beds in most hospitals, more than 20 percent of all nosocomial infections are acquired in ICUs [1]. ICU-acquired infections account for substantial morbidity, mortality, and expense. Infections and sepsis are the leading cause of death in noncardiac ICUs and account for 40 percent of all ICU costs [2].

When prescribing antimicrobials, the ICU clinician often faces a dilemma. In first place the traditional symptoms and signs of infection (such as characteristic patient history, fever, increased white cell count, etc) are common in ICU patients even in the absence of infection, making distinction of infectious and noninfectious causes of patient deterioration difficult. Secondly, delaying antimicrobial therapy, prescribing inadequate antimicrobials, or leave untreated bacterial infections increases patient mortality [5–7] resulting in guideline recommendations to start broad-spectrum antimicrobials as soon as possible in the presence of suspected severe sepsis [8]. On the other hand unnecessary antimicrobial therapy increases the risk of antimicrobial-related complications, such as *Clostridium difficile* colitis (with a crude mortality of up to 20% [9] and potentially endangers the greater population of ICU patients by increasing the prevalence of resistant organisms. Choosing between delaying necessary antimicrobial therapy

and exposing the patient to unnecessary therapy requires that these contrasting risks to be balanced—that of untreated infection versus late antimicrobial complications.

The main aim of this study was to assess how often administration of antibiotics for suspected infection could be justified by the presence of infection. The primary outcome measure was accuracy of antibiotic administration, defined as the proportion of antibiotics started for suspected infection where infection was later proven to have been present.

Indications for the use of antimicrobials in critically ill patients are similar to those for other hospitalized patients. However, the selection of agents depends on the particular characteristics of patients in the intensive care unit, signs and symptoms of infection, the type of infection and the bacteriological features of the causative pathogens.

2. Literature Survey

The use of antimicrobials in patients admitted to medical-surgical ICUs varies between 33 and 53% [3]. The selection of empirical antimicrobials to be included in treatment protocols of the most common infections depends on the strong interrelationship between patient characteristics, predominant pathogens in each focus, and antimicrobials used for treatment. Epidemiological studies carried out in the past have identified the microorganisms most frequently

responsible for community-acquired and nosocomial infections in patients admitted to ICUs [4]. Susceptibility to antimicrobial agents may be different between each geographical area, between each hospital and even within the same hospital service. In addition, susceptibility patterns may change temporarily in relation to the use of particular antimicrobials or in association with other unknown factors so that assessment of endemic antimicrobial resistance patterns is very useful in order to tailor the antimicrobial regimens of therapeutic protocols. Antimicrobial use should not be a routine procedure. The clinical course of the patient (an indicator of effectiveness) should be closely monitored as well as the possible appearance of adverse effects and/or multiresistant pathogens [5]. Controls are based on the assessment of plasma drug concentrations and microbiological surveillance to detect the presence of multiresistant strains or new antibacterial-resistant pathogens. Prevention of the development of multiresistant pathogens is the main goal of the ICU antimicrobial policy. Although a series of general strategies to reduce the presence of multiresistant pathogens have been proposed, the implementation of these recommendations in ICUs requires the cooperation of a member of the intensive care team. Every intensive care unit should have well-structured guidelines on the use of antimicrobial agents to guarantee that patients requiring intensive care receive appropriate antimicrobials for a relevant period to prevent and treat infections [6]. These guidelines should meet the therapeutic needs of the consultants and allow the infectionist, clinical microbiologist, and pharmacist to monitor efficacy, toxicity, including allergy and diarrhea, and side-effects, such as the emergence of resistant strains and subsequent outbreaks of superinfections. Calculation of infection rates is only feasible following the implementation of an antibiotic policy [7]. Apart from audit and research, antimicrobial guidelines aid educational programs and enable the clinical pharmacist to control drug expenditure. The main feature of an antibiotic policy in the ICU is the use of a minimum of well-established antimicrobial agents that are associated with a minimum of side effects, but also allow the control of the three patterns of ICU infections due to the 15 potentially pathogenic micro-organisms [8].

The aim of this study was to determine antibiotic usage patterns in the ICU and to compare the practices with international standards to identify areas for improvement.

3. Methods

Hospital Setting

A point prevalence study was conducted at four ICUs at University Hospital Centre "Mother Teresa" in Tirana, Albania which an overall capacity of 50 beds; Infectious diseases ward with 5 beds (10%), neurological ward with 14 beds (28%), cardiological ward with 19 beds (38%) and general ICU with 12 beds (24%) beds. Data was collected using a ward form and a patient form referring to the Global Point Prevalence Survey (Global PPS) methodology [9]. The patient form was fulfilled 'only' for those inpatients on antibiotic treatment at at 8 a.m on the day of the survey. However, all patients whether or not on antibiotic treatment were counted as the total number of patients (denominator data). The survey included all inpatients receiving an

antibiotic on the day of PPS. Data collected included age, gender, weight, antibiotic agents, doses, reasons and indications for treatment, compliance to guidelines and documentation of reasons. Denominators included the total number of inpatients. Patients were completely anonymized. Every patient record was given a unique not identifiable survey number.

Statistical analysis

Data was analyzed using SPSS version 19.0 software. Chi-square tests were used for comparing the percentages between variables. P-value ≤ 0.05 was considered as significant.

4. Results

Overall, 49 patients were included in the study from all ICU units. The mean age was 63.7 ± 14.5 years (range 28-86 years old); 52.5% were males and 47.5% females. The mean duration of ICU stay was 4.0 ± 3 days (range 1 to 11 days). Patients with a wide spectrum of clinical conditions were admitted and multiple and complex diagnosis was often observed. Cardiovascular diseases (31%), cerebrovascular accidents (22%), septicemia (17%), respiratory infections (15%), and febrile illnesses (11%) were among the most commonly encountered medical conditions. About 50% of the patients had a comorbidity. Hypertension was the most commonly found comorbidity followed by diabetes mellitus and ischemic heart disease. A total of 17 antibiotic agents were used with an average of 1.4 antibiotics per patient. In our study, 8 patients out of 49 (16.3%) did not receive any antibiotic, whereas the remaining 41 patients (83.7%) received one or more antibiotic. Table 1 shows the frequency of individual antibiotics. Regarding the availability and the use of guidelines they were missing in 36 cases (73.5 %). In 47 (96%) patients the antibiotics were administered parenterally (table 2).

Table 1: Prescription frequency of individual antibiotics

Antibiotic	ATC code	N	%
Ceftriaxone	J01DD04	8	16.3
Piperacillin/tazobactam	J01CR05	6	12.2
Ciprofloxacin	J01MA02	7	14.3
Amoxicillin/clavulanic	J01CR02	5	10.2
Azithromycin	J01FA10	4	8.2
Clindamycin	J01FF01	3	6.1
Cefoperazone/sulbactam	J01DD62	2	4.1
Doxycycline	J01AA02	2	4.1
Meropenem	J01DH02	2	4.1
Levofloxacin	J01MA12	2	4.1
Amikacin	J01GB06	2	4.1
TMP/SMX	J01EE01	1	2.0
Cefotaxime	J01DD01	1	2.0
Vancomycin	J01XA01	1	2.0
Ampicillin	J01CA01	1	2.0
Ceftazidime	J01DD02	1	2.0
Gentamycin	J01GB03	1	2.0

Table 2: Hospital indicators of antibiotic use

Indicators	N	%
Reason written in notes	46	94.0
Discontinuing /review date	4	8.2
Guidelines missing	36	73.5

Parenteral use	47	96.0
Targeted treatment	17	34.7

Empiric antibiotics were chosen most frequently to ensure coverage of the likely organism based on presumed source of infection. The most commonly prescribed culture-directed antibiotic was ceftriaxone (10.2%) followed by ciprofloxacin (8.2%), and meropenem (4.1%). 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 39% of cases, and hence became culture-directed. In 24% of cases, no reason could be found for continuing empiric therapy. The most common reason for the choice of prophylactic antibiotics was “based on experience” (23.8%). Meropenem and piperacillin/ tazobactam were chosen for their high powered, broad spectrum profiles. Reason for the use of the selected antibiotic was written in notes in 46 (94%) of cases. The discontinuing/review date was available for 4 (8.2%) of cases. Targeted treatment was found for 17 (34.7%) of patients. Of the total of patients, 13 (26.5%) were found to use combined antibiotics.

Studies have identified prior administration of antibiotics as a potential risk factor for inadequate antimicrobial treatment of infections [10]. This practice appears to predispose to colonization with bacteria that are often resistant to the previously prescribed classes of antibiotics [11]. The majority of patients (79.6%) 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 [12]. To be effective, the antibiotic selected should have activity against those organisms most likely to cause infection [13]. 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. 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 39% of cases. The practice of intravenous to oral switch therapy is a relatively new one in ICU. The antibiotics administered orally are those with documented high bioavailability and have few gastrointestinal side effects [14,15]. 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 [16].

5. Conclusion

In ICUs, broad spectrum antibiotics are widely used to treat critically ill patients undergoing surgical procedures. Due to the large number of healthcare workers and the possible

transmission of pathogenic bacteria from patient to patient, ICUs are high-risk wards with for the spread of antibiotic-resistance bacteria. Strategies to reduce antibiotic prescribing are therefore needed and should include an immediate diagnostic process before starting early probabilistic antibiotic therapy in case of severe sepsis or septic shock.. Combination therapy is suggested for patients with septic shock and neutropenia or in patients at high risk of multidrug-resistant bacterias. Prompt collection of culture reports and early set-up of a culture directed antibiotic regime, including a possible de-escalation when possible is imperative. This will require early and regular consultation with the Microbiology Department to identify common isolates, their antibiotic sensitivity by antibiograms and the appropriate treatment protocol. In contrast, in the absence of severe sepsis, waiting for objective data to diagnose infection before treatment with antibiotics for suspected ICU-acquired infections does not worsen mortality and might be associated with better outcomes and use of antimicrobial drugs and should be discussed on daily rounds.

6. Future Scope

These data suggest that an Antibiotic Control Policy needs to be established in the ICUs and a multidisciplinary approach should be developed for a correct and specific antibiotic administration.

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thesis entitled: "Antibiotic use and Stewardship in Health Care Institutions in Albania". During my academic carrier, in 2013-2015 I have held full course lectures at the University of Sports in Tirana, in subjects "Doping, supplements and nutrition integrators in sports" and Biology and Biochemistry of Physical Activity. My working experience started in April 2012 as a Regulatory Affairs Specialist at Pharmaceutical Company "Profarma sh.a.", Tirana (Albania) and after October 2013 as a Quality Assurance Specialist at the same company. Since August 2015, she applied and won the position as Pharmacy Course Coordinator and academic assistant and Full – time Member of the Department of Chemistry – Pharmaceutical and Bio-molecular Technologies at the Faculty of Pharmacy of Catholic University "Our Lady of Good Council", Tirana, Albania. She has participated in several national and international pharmaceutical conferences. She obtained an observership grant from the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) for a short term research at the University Hospital for Infectious Diseases in Zagreb, Croatia and I am a full member of the ESCMID. She have excellence proficiency in Italian Language, very good in English and Spanish Languages.

Author Profile



Silvi Bozo during 2006-2012 have followed the University studies in an integrated Master of Science (five years course) in "Pharmacy and Industrial Pharmacy and obtained the Double Degree in "Pharmacy and Industrial Pharmacy" from the University of Milan, Italy and Catholic University "Our Lady of Good Council", Tirana, Albania. In May 2012 held successfully the state professional exam for Pharmacists. During her studies she have obtained study grants and won the prize "Premio di Ricerca in memoria della Prof.ssa Sottocornola" for excellent results. Since November 2014 and on, she is a PhD Candidate at the Doctoral study program in "Public Health, Molecular diagnosis of Infectious Diseases and Pharmacovigilance" at University "Our Lady of Good Council", Faculty of Pharmacy, Tirana (Albania), with a PhD