

ASSESSMENT OF RESISTANCE AND ADVERSE EFFECTS OF REPEATED ANTIBIOTIC PRESCRIPTION AND ITS CORRELATION WITH HOSPITAL ADMISSION

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Abstract

Background: Infections usually are linked to multi-resistant a germ which is considered a global health problem, repeated antibiotic prescription practices give the chance to assess and establish programs for encouragement of ideal use of antibiotics that help in improvement of quality of care. The major disease which need antibiotic on admission of hospital and need health care are pneumonia, urinary tract infection, and skin and soft tissue infection which need type of antibiotic have resistance so these diseases should be the key pathologies for the programs of antimicrobial management. **Material and methods:** it is observational, descriptive, cross-sectional study for duration of 3 months with patients admitted to the Pediatric Specialty Hospital with diagnoses of diseases of pneumonia, urinary tract infections and skin infections

Results and conclusions: 127 subjects were eligible. 16.5% of these lacked hospitalization criteria, the choice of empirical antibiotic was in accordance with that recommended by the guidelines in 78.7% of the patients, subjects received prescribed antibiotics at the appropriate doses and intervals. 66.1% were compliant criteria for sequential therapy, it was performed in 7.9% of the cases. The infectious disease recommendations they were followed by the treating physician in 68.7% of the cases. The study points out the importance of establishing programs and strategies within primary care and hospitalization criteria, as well as establishing antibiotic management policies to minimize over side effects and resistance of prescribed antibiotics

Keywords: Antibiotic resistance, repeated prescription of antibiotics, hospital admission, primary care.

Introduction:

The advent of antibiotic therapy in the 1940s has completely revolutionized the medical field and resulted in a significant reduction in mortality associated with infectious diseases. Unfortunately the bacterial resistance to traditional antibiotics has quickly become a major health problem in worldwide. Resistance to penicillin due to over prescription has developed in the 1950s, to cephalosporins of first generation in the 1970s and cephalosporins third generation in the 1990s.(1)

In recent years, the frequency and extent infections caused by resistant bacteria (2) have increased as much in

hospitals as in community, so it need hospital admission and primary care.

We can now observe resistance in almost all bacteria potentially pathogens. There are about 25 million prescriptions of antibiotics written annually in Canada, and we considers that more than 50% of prescribed antibiotics would be inappropriate, so it is not surprising to observe the development of resistance.

Hospitalized people are particularly vulnerable to the transmission of resistant bacteria, especially in intensive care units. It is estimated that 60% of nosocomial infections worldwide are caused by resistant bacteria1. In North America, about a third of patients hospitalized

receive an antibiotic during their stay hospital (3-15). Inappropriate and over prescribed use of antibiotics in prophylaxis varies between 40% to 75% depending on the various studies, and 30% to 75% of patients with pulmonary infiltrates receive antibiotics for a non-infectious cause. Unnecessary exposure to antibiotics not only increases the risk of toxicity to the patient, such as side effects, drug interactions, super-infections, prolongation of illnesses and even death, but is also mainly responsible for the emergence of resistance. The link between the use of antibiotics and the emergence of bacterial resistance is clear: the indiscriminate use of antibiotics promotes the emergence of bacterial resistance

Prevention of resistance: Role of the physicians and hospital

The emergence of resistance, although it is a phenomenon natural adaptation of microorganisms to their environment, can be accelerated by various factors. (4) Any misuse of antimicrobials, misuse and treatment too short, any insufficient dosage, potency too weak and disease not relevant for the drug in question considerably increase the probability that the bacteria or other microorganisms adapt and multiply instead of disappearing. As physicians, we need to make sure that the antibiotics are used appropriately. The informed use of antibiotics is defined as the optimal selection of the agent, the dose and the duration of the antibacterial treatment nothing resulting in the best clinical course in terms of therapy or prevention, with the least toxicity and impact on resistance(4).

For all these reasons, improving the employment of these drugs is a priority if we want to fight against the emergence and spread of resistance. In establishment health care systems, we must ensure that our distribution of antibiotics are well suited, set up to avoid prolonged treatments unnecessarily, may conversely, cause a delay in renewing prescriptions antibiotics for serious infections and thus promote the emergence of resistance if the wait is extended. The pharmacist should also participate actively in multidisciplinary committees promoting the appropriate use of drugs and prevention of infections

Prevention strategies

Prevention of resistance should be carried out according to a multidisciplinary approach. Many strategies for preventing or delaying the emergence of resistance and it is within the role of hospital and primary care:

Quantitative and qualitative monitoring of the use of antibiotics

In order to promote the appropriate use of anti-infectives and thus prevent the emergence of resistance, implementation of quantitative monitoring programs and qualitative use of antibiotics in Quebec health institutions

is paramount. (SHEA) (13) and (IDSA) states that the reducing the consumption of antibiotics is one of the most important measures to combat development of resistance. A frame of reference provincial policy on the optimal use of anti-infectives and monitoring the use of these drugs in the environment hospital was recently published by the Council of drug.(14)

Methodology

An observational, descriptive, cross-sectional study was carried out. The files of subjects who entered hospital rooms were reviewed. hospitalization of the Hospital de Especialidades Pediátricas Omar Torrijos Herrera with the diagnoses of pneumonia, infection of urinary tract and skin and soft tissue infection during period from October to December 2016. The samples were calculated for each pathology. In the pneumonia group for a population of 122 patients (last quarter of 2015) was obtained a sample of 93 individuals with a level of confidence 95%, using the STATCALC program included in Epi Info 7.2.0.1. For the UTI and Skin and tissue infection groups soft took the whole universe.

Subjects under 15 years of age who were admitted to hospital wards with a diagnosis of pneumonia, urinary tract infection, or skin and tissue infection receiving antibiotics.

The subjects admitted to the intensive care unit, hospitalized in the observation area and discharged from that ward and subjects with hemato-oncological diagnoses, congenital or acquired heart disease, immunodeficiency congenital or acquired, nosocomial infections, paralysis infantile brain, cystic fibrosis, tracheostomized or with other chronic lung diseases.

The Epi Info 7.2.0.1 program was used to create the database data and its analysis. For the qualitative variables, frequency distributions. Tables and graphs were designed using Microsoft Office Excel 2013 program 15.0.4815.1000 64-bit and for the presentation the Microsoft Office PowerPoint 15.0.4811.1000 64-bit program.

The study received approval from the Hospital authorities Pediatric Specialties Omar Torrijos Herrera and the Committee Institution of Ethics in Research of the Insurance Fund Social.

Results

A total of 155 files were reviewed, 127 patients were eligible (**See Table 1**). The predominant age group It was from 1 to 4 years old and 80% male (**See Table 1**). So Overall, the selection of the empirical antibiotic was in accordance with recommended by the guidelines in 78.7% (100/127) of the patients.

Table 1: **Characteristic of participants in this study**

Age	total%
Less than one year	35 (27.6%)
1-4	64(50.4%)
5-9	17(13.4%)
10-15	11(8.7%)
Gender	
Male	80(63%)
Type of infection	
Pneumonia	93(73.2%)
UTI	8(6.3%)
Skin infection	26(20.5%)

Of the 27 patients in whom the chosen antibiotic empirically it was not in accordance with the guidelines, 77.8% were patients without criteria for hospitalization who could have been managed outpatiently with oral antibiotics.

100% of the patients received antibiotics prescribed in the regulated doses and intervals. The way of the predominant administration was the intravenous route (99.2%). Being penicillin the family of antimicrobial used with more frequent, followed by cephalosporins

The date of review of the indication of antimicrobial therapy in 4 (3.1%) patients. Of the 127 patients, 66.1% met criteria for therapy sequential at 72 hours

Average hospitalization time was 6.4 days, with a minimum of 3 days and maximum of 11 days . The duration of antimicrobial therapy considering the days of hospital treatment and prescription of antibiotics at discharge. I calculated the mode for treatment days resulting in pneumonia 10 days, UTI 7 days and skin and soft tissue infection 7 days.

Blood culture was taken in 101 patients (79.5%). The taking blood culture was indicated in 76.4% of the patients. A blood culture was taken prior to the start of antibiotics in 86.1% (87/101) of the cases. There was no growth of microorganisms in none of the blood cultures taken. 16 patients (12.6%)

They were evaluated by Infectology. All of the consultations were requested for antibiotic approval broad spectrum. The recommendations were followed by the treating physician in 68.7% of the cases.

In cases where the recommendations were not followed by the treating physician, Infectology recommended reducing the antibiotic spectrum and / or perform sequential therapy, which was performed in 7.9% of the cases.

In pneumonia, 116 records were evaluated with pneumonia as an admission diagnosis, 23 patients did not had entry criteria for the study, 10 (43.5%) patients

presented some type of comorbidity, 4 (17.4%) did not qualify for being patients transferred to the ward of the care unit

intensive, 2 (8.7%) left the study as they were transferred to intensive care unit for the first 72 hours hospitalization and 7 (30.4%) did not meet diagnostic criteria for pneumonia. Of the 20 patients in whom the antibiotic chosen empirically was not in accordance with the guidelines, 75% did not had admission criteria and could have been treated outpatient with oral antibiotics, the remaining 25% were given indicated a broad spectrum antibiotic without having criteria of complicated pneumonia. Infectology evaluated 9 patients for broad spectrum antibiotic approval, recommended continue with the antibiotic in 5 patients who had criteria of complicated pneumonia and decrease the antibiotic spectrum in 4 remaining; this recommendation was followed in all 4 patients.

Blood culture was taken from all patients, however, 15% (14/93) was taken after the start of antibiotics. 62.4% of patients had criteria for timely sequential therapy, it was performed in 7.5% of the cases.

For urinary tract infection, 13 files were reviewed reported with urinary tract infection as diagnosis of admission, 5 patients did not meet the criteria for admission to study, 3 patients younger than 3 months presented symptoms of February without other symptoms and pathological urinalysis taken by collection bag from which no urine culture was repeated or taken with aseptic technique, 2 patients had urine culture taken with aseptic technique prior to starting antibiotics without isolation of microorganism in urine culture. Infectology evaluated 7 patients of the 8 diagnosed with UTI, in 4 patients it was recommended continue with empirical antibiotic and switch to oral route if met criteria for timely sequential therapy.

Infectology recommendations were followed in 42.9% of the cases. 87.5% of patients met criteria for therapy sequential. Timely sequential therapy was performed in 37.5% of the cases. Blood culture was taken in all 8 patients. In just 4 cases, blood culture taking was indicated according to the rule. No microorganism was isolated in blood cultures

The microorganism isolated in 100% of the urine cultures was *Escherichia coli*, which was sensitive to the empirical antibiotic and lower spectrum antibiotics in all antibiograms. I know the antibiotic spectrum decreased by 37.5% (3/8).

The 26 patients diagnosed with skin and tissue infection soft entered the study. The prescribed empirical antibiotic was not in accordance with that recommended by the guidelines in 23% of the patients, of these 100% lacked

criteria for hospitalization. Evaluation by infectology was not requested in none of the patients. 73.1% of the patients had criteria for sequential therapy. Sequential therapy was not performed timely in none of the patients.

For the year 2016, the average hospital bed day in the pediatric medicine ward of HEPOTH it was estimated at B /. 374.08. In pneumonia, 12% (7/58) of patients with criteria for sequential therapy were changed to oral, prolonging the hospital stay, and increasing B /. 57,234.24 to hospitalization costs. In IVU 43% (4/7) of the patients with criteria for sequential therapy were performed change to oral route, prolonging the hospital stay, and increasing B /. 5,985.28 to hospitalization costs.

In skin and soft tissue infection 0% (0/19) of patients with criteria for sequential therapy, they were changed to via oral, prolonging the hospital stay, and increasing B /. 17,207.68 to hospitalization costs.

Discussion

It is currently proven that the use of antibiotics is the most important risk factor in the development of bacterial resistance. Of numerous studies have shown the preponderant role antibiotics in the emergence of resistance. In antibiotics work on several levels: they can transform the patient's normal flora, promote colonization by resistant bacteria and facilitate their dissemination. This selection pressure is all the more marked as the number of patients treated is important and the hospital stay is long.

Antimicrobial resistance has serious consequences having major impacts on both quality of care over patients and costs. The bacterial resistance leads to increased morbidity, mortality and health care costs, caused by longer hospitalizations and need to use more expensive drugs and often more toxic.

Antimicrobial resistance is widely considered, as one of the main public health problems. The optimal prescription of antibiotics is required to the treatment and prophylaxis of infectious diseases, as well as to avoid the development of antimicrobial resistance and effects adverse reactions related to the use of antimicrobials. Community scientist makes a particular call to improve the capacity of clinical and laboratory diagnosis of diseases infectious.(5)

Optimizing the use of antimicrobials begins with the correct and timely diagnosis, which requires techniques diagnostic novelties as a chain reaction of real-time polymerase and assisted laser desorption / ionization by matrix (MALDI-TOF). In our study 7.7% (12/155) of cases admitted with a diagnosis of pneumonia and UTI do not they met diagnostic criteria.

In the pneumonia group 43% (3/7) of the patients without diagnostic criteria lacked radiographic findings that

support the diagnosis, which correlates with found in a prospective observational study(6)

Acute phase reactants such as C-reactive protein (CRP) and procalcitonin (PCT) have been traditionally used as diagnostic tools in infectious processes.

In the last decade, more data has been obtained on the role specific to these markers. This includes the potential role in early diagnosis, differentiation of bacterial causes and prognostic marker in counseling strategies antibiotic. These tools should be used with caution depending on the type of infection and specific cut-off value. It has been described its low positive predictive value (PPV) in pneumonia; by example was found in a systematic review that assesses the Diagnostic value of CRP in respiratory tract infections lower bacterial etiology found sensitivities in ranges from 8 to 99% and specificities from 27 to 95%, making the

PCR a test neither sensitive enough to rule out nor specific enough to confirm an etiology bacterial.(7)

Unlike its performance in pneumonia, the usefulness of PCR and PCT as diagnostic tools in UTI have shown to be high, for example, Xu et al found that PCT and CRP values in children with acute pyelonephritis were significantly higher than those of children with tract infection lower urinary tract in addition the PCT values are correlated with the degree of renal involvement.11 The envelope diagnosis in UTIs is a common problem, leading to overuse of antibiotics. We found that 60% of the patients over diagnosed with UTI were sampled with collecting bag.

The development of rapid molecular diagnostic methods is a promising strategy to combat resistance antimicrobial. Fast and accurate agent detection etiological allows providing adequate treatment of early, improving clinical outcomes, shortening the duration of treatment and narrowing the spectrum of antimicrobial therapy. Pérez et al found that integration of rapid identification techniques and Susceptibility significantly improved the time to optimal therapy and decreased hospital stay and costs hospitalization totals. (8)

Taking cultures before starting antibiotics helps to direct therapy and optimize treatment duration and compliance with the guidelines. Taking blood cultures in patients with pneumonia have a poor performance, especially in children with uncomplicated pneumonia, becoming isolated

microorganisms in percentages as low as 2.2% in some studies(9), despite this it has proven to be useful for cost and antibiotic administration programs - effectiveness of medical decisions.

It was evidenced that 78.7% of the patients prescribed the adequate empirical antibiotic, a percentage higher than found by Aly et al in a retrospective study in 9 hospitals

where the choice of antibiotic was appropriate and according to the guidelines in 52.7% of the prescriptions.(10) In our study found that 77.8% of patients with choice inadequate empirical antibiotic had no criteria for admission, this implies that they could receive treatment.

It should be noted that, despite not present admission criteria, the treating doctors of the ward maintained in-hospital treatment in most of the patients. It is proven that prolonged hospitalizations increase costs and increase the risk of infections nosocomial and the incidence of iatrogenic procedures, without count indirect costs for example, Lee et al(11) in a study the impact of hospitalization for diarrhea on parents acute in children, found that the substantial loss of income due to absence from work and transportation were among the 3 higher expenses reported by parents and that the cost of hospitalization constituted approximately 16% of admission family monthly therapy. Timely sequential therapy was not performed in 88.1% (74/84) of the patients who had criteria for it.

These findings exceed those found in studies that evaluate causes of prolonged hospital stay, for example, a A prospective study of 2,762 patients found that 67% of patients patients with a delay in hospital discharge presented compatible clinical stability for discharge.(12) The prescription of antibiotics in the appropriate doses in our inpatient wards is a proven strength in this study with 100% adherence to the appropriate doses recommended by the guides, data similar to that found by Aly et al with 94% adherence to adequate doses recommended by the guidelines, (10) however, reevaluate the chosen antibiotic or need for spectrum change not is part of the routine within the management plan of the patients in our hospitalization rooms, since only 3.1% of the patients, the date of antibiotic therapy review.

Conclusions

The study indicates that the elements that affect the antimicrobial prescription characteristics affect the course of hospital stay of patients who they enter HEPOTH's inpatient wards. It is observed a significant percentage of patients admitted without diagnostic criteria and without admission criteria, which conditions the inappropriate choice of an antibiotic empirical and puts the patient at

risk of adverse effects related to health care, as well as an increase of health care costs. In the same way do, the absence of a management plan that optimizes the use antimicrobials.

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