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Antibiotic misuse and overuse in hospitalized patients with nosocomial infections in North of Iran

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Abstract

Background: Improper use of antibiotics increases the cost of treatment, incompetent therapy, longer hospitalization time, more visits to the doctors, and improper treatment of the patients, lack of infection control, and the development and spread of antibiotic resistance. The objective of this study was the evaluation of antibiotic misuse and overuse in hospitalized patients with nosocomial infections in BuAli Sina hospital, in the north of Iran.

Method: This retrospective cross-sectional study was performed by census methods on all nosocomial infections patients hospitalized in BuAli Sina's educational and therapeutic hospital. Data were collected from March 2016 to March 2018. All data were obtained from computerized archives and manual archives of the hospital. SPSS 16.0 was used for statistical analysis using Chi-square, Kolmogorov-Smirnov, and Mann-Whitney tests.

Result: Out of 517 patients studied, 221 (42.7%) of them were male. The average age of the patients was 45.64±34.01. The Most Common isolated bacteria from all patients were Escherichia coli (48.8%) and Staphylococcus epidermidis (22.9%). According to the antibiotic prescription in the present study, most patients (35.8%) took at least two antibiotics. The most antibiotics falsely prescribed by physicians in the present study were used for the treatment of the infections caused by E. coli (50.34%) and Klebsiella pneumoniae (20.97%).

Conclusions: There seems to be a need to set up a team to prevent antibiotic misuse and microbial resistance and to pay attention to the antibiotics prescribed for infectious patients. These include training programs for physicians, consulting with infectious disease specialists, reducing empirical prescriptions by physicians, and spontaneous antibiotic use by patients.

Keywords:
Inappropriate Antibiotics, Misuse, Overuse, Antibiotics prescription, Infectious diseases,

Introduction

Antibiotics introduced in the 1940s, and from that time up to now, these antimicrobial agents have been used as the primary treatment options for bacterial infections. However, by the time passing, inappropriate use of them led to serious and global concerns (1). Antibiotics are very effective antimicrobial drugs, necessarily in developing countries where infectious diseases are still the most causes of death (2). These antimicrobial agents

are decreasing the rate of mortality and morbidity, while the misuse and overuse of these drugs can lead to dangerous effects such as the resistance of some microorganisms to them (3, 4).

Antibiotics are the second prevalent prescribed drugs in many hospitals in the USA and Europe (5). While 60-90% of the infectious patients receive antibiotics, 40% of prescriptions are usually without laboratory confirmation (5). The rate of antibiotics usage in surgical settings is higher than that of internal medicine, while most cases of antibiotic usage are for prophylaxis (5). These antibacterial agents are the largest group of drugs purchased in developing countries regarding their easy availability and poor control (6). It seems that restriction programs such as standard prescription of these drugs by physicians, government control on selling these drugs, education for the people, and policies for the restriction use of antibiotics in hospitals can be useful to decrease the antibiotic usage in these countries (6).

In Iran, the average consumption of medications is 2 to 4 times higher than its use in the USA and Europe (7). Acetaminophen and antibiotics (mostly for the treatment of upper respiratory tract infections) are the most common medications prescribed by physicians (7). Some more common infectious diseases for antibiotic prescription were the infection of respiratory tracts, wounds, gastrointestinal tracts, eyes, ears, and urinary tracts (8). The most common antibiotics used for the treatment and sometimes self-medication included amoxicillin, macrolides, fluoroquinolones, cephalosporins, and metronidazole (9). There are many reasons for this tendency, including the patient's wrong beliefs in using unnecessary drugs, doctor's propensity for prescription many requested medications for satisfying their patients, uncertainty about antibiotic responsiveness against the infections, and the lack of trust in the laboratory results (7).

Center for Disease Control and Prevention (CDC) estimated that 20-50% of all medical prescriptions are unnecessary and inappropriate (1, 10). On the other hand, when patients feel healing or have specific side effects caused by the antibiotics, they begin to stop using them (11). Inappropriate use of antibiotics such as uncompleted therapy, not regarding dosage or re-using of remaining antibiotics, can expose patients to different dosages of antibiotics. This inappropriate behavior leads to a lack of antibiotics' potency to eliminate the infections caused by bacteria, increasing the risk of antibiotic resistance. Also, improper use of antibiotics increases the cost of treatment, incompetent therapy, longer hospitalization time, and more visits to the doctors (11, 12). Moreover, many reasons have reported for the misuse of antibiotics. For example, many hospitals do not have an infectious disease specialist (13), or a

pharmacist trained in the field of infectious diseases (14). Health workers, managers of health centers, health organizations, educational institutions, and people must help to solve the problems. It seems that the main focus should be on the education of medical, pharmacological, and graduate students (15).

As, the appropriate use of antibiotics is very important for accurate treatment of patients, proper infection control and prevention of the development and spread of antibiotic resistance, the purpose of this study was to comprising the antibiotic prescription in an educational and therapeutic hospital, BuAli Sina, in the north of Iran to find out the rate of overuse and misuse of antibiotics.

Methods

This retrospective cross-sectional study was performed by using available data and census methods on all nosocomial infections hospitalized in BuAli Sina hospital(affiliated to the Mazandaran University of Medical Sciences, Sari, in the north of Iran). Data were collected from March 2016 to March 2018. In this study, 517 patients were included as they had an infection and used the antibiotics during the hospitalization period. The exclusion criteria of the study were the incomplete medical records and patients without bacterial infections.

Two of our team members referred to the department of medical records of the BuAli Sina hospital to complete the checklists for available information. The checklists included age, gender, type of infection, antibiotics prescribed for the patient's disease, sample type (the sample which had taken from the patients include: blood, urine, and wound), hospital ward, and the results of antimicrobial susceptibility testing. All data were obtained from computerized archives and manual archives of the hospital. Finally, we investigated the antibiotics prescribed for the patients' infections according to the criteria of the Clinical and Laboratory Standards Institute (CLSI) (16), and Harrison's Principles of Internal Medicine (17) and Mandell Douglas, and Bennett's Principles and Practice of Infectious Diseases (18) for measurement right prescription and right usage of the antibiotics.

At first, Microsoft excel 2016 was used to categorize the extracted data, and then the Statistical Package for the Social Sciences 16.0 (SPSS 16.0 Inc. Chicago, IL, USA) was used for statistical analysis using *Chi*-square, Kolmogorov-Smirnov and Mann-Whitney tests.

Ethical consideration

The ethics committee of Mazandaran University of Medical Sciences has approved the present study by IR.MAZUMS.REC.1398.001 ethical

code, which adopted Feb 20, 2018. All information contained in the medical records archives were used confidentially and exclusively for the aim of this study, and all files were delivered to the department without any changes.

Results

Out of 517 patients studied, 221 (42.7%) of them were male, and 297 (57.4%) patients were female. The average age of the patients was 45.64±34.01 (from 1-94-year-old).

The most common isolated bacteria from all patients were Escherichia coli (48.8%), Staphylococcus epidermidis (22.9%), Klebsiella pneumonia (12%), Pseudomonas aeruginosa (8.3%) and Staphylococcus saprophyticus (4.2%).

Among all 517 patients that had completed data, the most prevalent (32.1%) age group of the study was less-than-ten-year-old (Table 1). Moreover, the most prescribed antibiotics were seen in the less-than-ten-year-old group, too (Table 1). Also, we have 28 cases who hadn't prescribed any antibiotics for them despite the laboratory found infection in their samples.

According to the antibiotic prescription in the present study, most patients (35.8%) took at least two antibiotics, while 26.8% and 21.2% of the patients received one, and three antibiotics for the treatment of the bacterial infection, respectively. Also, among all 571 patients with various age groups, the most prescribed antibiotics were ceftriaxone (28.2%), meropenem (14.7%), and amikacin (11.2%), respectively (Table 1).

Except for ceftriaxone, there was no significant correlation between the gender of the patients and the type of antibiotics prescribed (Table 1).

Table 1. Frequency of patients and prescribed antibiotics across age groups and different genders

Age groups	<=10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	91-100	Total	Gender	
Frequency	166 (32.1%)	18 (3.5%)	14 (2.7%)	10 (1.9%)	21 (4.1%)	34 (6.6%)	68 (13.2%)	92 (17.8%)	87 (16.8%)	7 (1.4%)	517 (100%)		
Antibiotics												Male	Female
Ceftriaxone	92 (30%)	15 (5%)	10 (3.3%)	9 (3%)	9 (3%)	17 (5.6%)	41 (13.6%)	49 (16.2%)	55 (18.2%)	5 (1.6%)	302 (28.2%)	112	190
Meropenem	38 (24%)	15 (9.5%)	7 (4.4%)	2 (1.3%)	4 (2.6%)	9 (5.7%)	26 (16.5%)	30 (19%)	25 (15.8%)	2 (1.3%)	158 (14.7%)	76	82
Amikacin	59 (49%)	4 (3.3%)	1 (0.8%)	1 (0.8%)	0 (0%)	5 (4.2%)	12 (10%)	20 (20%)	16 (13.3%)	2 (1.7%)	120 (11.2%)	54	66
Ciprofloxacin	46 (48.4%)	3 (3.1%)	0 (0%)	2 (2.1%)	0 (0%)	6 (6.3%)	15 (15.8%)	18 (19%)	5 (5.3%)	0 (0%)	95 (8.9%)	49	46
Vancomycin	32 (32.3%)	3 (3%)	5 (5%)	0 (0%)	6 (6%)	6 (6%)	10 (10.1%)	17 (17.2%)	14 (14.1%)	3 (3%)	96 (9%)	54	42
Metronidazole	13 (10.7%)	1 (0.8%)	5 (4.1%)	3 (2.5%)	1 (0.8%)	4 (3.3%)	18 (14.8%)	20 (16.4%)	12 (9.9%)	1 (0.8%)	78 (7.2%)	31	47
Clindamycin	12 (16.7%)	2 (2.8%)	0 (0%)	1 (1.4%)	4 (5.6%)	8 (11.1%)	7 (9.7%)	13 (18%)	25 (34.7%)	0 (0%)	72 (6.7%)	30	42
Azithromycin	0 (0%)	0 (0%)	2 (6.2%)	4 (12.5%)	1 (3.1%)	2 (6.2%)	6 (18.8%)	8 (25%)	9 (28.1%)	0 (0%)	32 (3%)	18	14
Ampicillin	16 (66.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (8.3%)	6 (25%)	0 (0%)	24 (2.2%)	10	14
Other	52 (54.7%)	4 (4.2%)	0 (0%)	0 (0%)	3 (3.1%)	8 (8.4%)	8 (8.4%)	7 (7.4%)	13 (13.7%)	0 (0%)	95 (8.9%)	46	49
Total	360 (36.6%)	47 (4.4%)	30 (2.8%)	22 (2%)	28 (2.6%)	65 (6%)	143 (13.3%)	184 (17.1%)	180 (16.8%)	13 (1.2%)	1072 (100%)	480	592

The highest rate of antibiotics' prescription, in terms of hospital wards, was observed in internal medicine, ICU, Neurology, and emergency, respectively (Table 2).

Moreover, ceftriaxone and meropenem were the most prevalent antibiotics for patients hospitalized in the ward of neurology, while ceftriaxone alone was a significant option in the internal ward.

Table 2 Frequency of antibiotics' prescription in terms of hospital wards

Antibiotics	Neurology	Emergency	Neonates	Pediatric Infection	Pediatric	Internal medicine	Pediatric Surgery	ICU	PICU	NICU	ENT	ENT	Oncology	ophthalmology
Ceftriaxone	52 (34.43%)	47 (30.71%)	0 (0%)	41 (58.57%)	19 (48.71%)	65 (38.69%)	27 (45%)	32 (20.77%)	2 (6.66%)	0 (0%)	3 (37.5%)	7 (35%)	6 (26.08%)	1 (100%)
Meropenem	30 19.86%)	20 (13.07%)	6 (15.78%)	3 (4.28%)	0 (0%)	18 (10.71%)	2 (3.33%)	35 (22.72%)	9 (30%)	15 (25%)	1 (12.5%)	2 (10%)	7 (30.43%)	0 (0%)
Amikacin	9 (5.96%)	10 (6.53%)	12 (31.57%)	8 (11.42%)	8 (20.51%)	17 (10.11%)	17 (28.33%)	2 3 (14.93%)	3 (10%)	12 (20%)	0 (0%)	2 (10%)	0 (0%)	0 (0%)
Ciprofloxacin	1 (0.6%)	3 (1.96%)	0 (0%)	2 (2.85%)	3 (7.69%)	3 (1.78%)	0 (0%)	3 (1.94%)	1 (3.33%)	0 (0%)	1 (12.5%)	0 (0%)	0 (0%)	0 (0%)
Vancomycin	9 (5.96%)	18 (11.76%)	7 (18.42%)	2 (2.85%)	2 (5.12%)	11 (6.54%)	2 (3.33%)	22 (14.28%)	7 (23.33%)	12 (20%)	0 (0%)	2 (10%)	3 (13.04%)	0 (0%)
Metronidazole	21 (13.90%)	16 (10.45%)	0 (0%)	0 (0%)	1 (2.56%)	18 (10.71%)	3 (5%)	7 (4.54%)	0 (0%)	9 (15%)	1 (12.5%)	2 (10%)	0 (0%)	0 (0%)
Clindamycin	13 (8.6%)	12 (7.84%)	0 (0%)	7 (10%)	1 (2.56%)	13 (7.73%)	2 (3.33%)	18 (11.68%)	1 (3.33%)	0 (0%)	1 (12.5%)	1 (5%)	3 (13.04%)	0 (0%)
Azithromycin	5 (3.3%)	12 (7.84%)	0 (0%)	0 (0%)	0 (0%)	13 (7.73%)	0 (0%)	2 (1.29%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Others	11 (7.28%)	15 (9.8%)	13 (34.21%)	7 (10%)	5 (12.82%)	10 (5.95%)	7 (11.66%)	12 (7.79%)	7 (23.33%)	12 (20%)	1 (12.5%)	4 (20%)	4 (17.39%)	0 (0%)
Total	151	153	38	70	39	168	60	154	30	60	8	20	23	1

In another point, we compared the antibiotics' prescriptions with the laboratory antimicrobial susceptibility testing (AST) results. We divided these antibiotics to different groups including the antibiotics that the bacteria were resistant, intermediate resistant, and sensitive to them, the antibiotics which prescribed correctly according to the AST, and the unknown antibiotics which physicians prescribed them even though they were not reported in the laboratory testing (Table 3).

Table 3. Frequency of different antibiotics prescribed according to the laboratory antimicrobial susceptibility testing.

Groups of antibiotics	Frequency of prescription No. (%)
antibiotics which the bacteria were resistant to them	143 (13.24)
antibiotics which the bacteria were intermediate resistant to them	12 (1.11)
antibiotics which the bacteria were sensitive to them	433 (40.09)
unknown antibiotics	492 (45.55)
Total	1080 (100)

According to the results of the above table, the prescription of the antibiotics in which the bacteria was resistant to them, according to the AST was certainly false. Also, we found that the most antibiotics falsely prescribed by physicians in the present study were used for the treatment of the infections caused by E. coli (50.34%), K. pneumoniae (20.97%), S. epidermidis (5.59%) and P. aeruginosa (5.59%), respectively (Table 4).

Table 4. Most cases of antibiotics' misuse for treatment of the bacterial infections

Bacteria that cause infections	False antibiotics' prescription No. (%)
Other Gram-negative bacilli	1 (0.7%)
Staphylococ cus epidermidis	17 (11.89%)
Staphylococcus aureus	2 (1.4%)
Streptococcus viridans	2 (1.4%)
Streptococcus pneumoniae	1 (0.7%)
Total	143 (100%)
Pseudomonas aeruginosa	11 (7.69%)
Acinetobacter baumannii	4 (2.79%)
Escherichia coli	72 (50.35%)
Klebsiella spp.	30 (20.98%)
Proteus spp.	1 (0.7%)
Enterobacter spp.	2 (1.4%)

Discussion

Antibiotic misuse in clinical settings is an important global problem (19). The antibiotics are a big part of hospital drug expenditures, generating unnecessary costs, and causing bacterial resistance (20). However, inappropriate use of antibiotics is a major factor for bacterial resistance. An important reason for incorrect use of antibiotics is the physicians' prescription based on experience without attention to the signs and symptoms and para-clinical tests, resulting in the increase of bacterial resistance rates and the costs of antibiotic therapy (21). The misuse and inappropriate use of antibiotics have been proven in several studies (22).

In a recent study between medical and non-medical students in the University of Malaysia has shown that more than half of them had low knowledge and used un-prescribed antibiotics without the following of the treatment (23). A study in Jordan investigated three patterns of dispensing antibiotics in a sample of community pharmacies and found that a significant proportion of the antibiotics were dispensed without prescription (21). Another study in China showed a high rate of antibiotics misuse by well-educated young adults in two regions (24). Cambodia is a country in which infectious diseases are common, and access to antibiotics is so easy there. A study in this country identified that self-medication with different antibiotics for mild illnesses is a big problem in Cambodia. The main driver of the community's demand for antibiotics in this country was a mistaken belief in the benefits of antibiotics for a common cold, high temperature, pain, malaria, and 'Roleak' which includes a broad catch-all for perceived inflammatory conditions. In conclusion, the investigator believes that it's better to limit the use of antibiotics, especially without prescription (25).

In our study, according to the role of bacteria in hospital infections, Escherichia coli (47.7%), Staphylococcus epidermidis (18.5%) and Klebsiella spp. (6.8%) were the most prevalent ones, similar to other epidemiological research (26). Our study showed that the most prescribed antibiotics were ceftriaxone (28.2%), meropenem (14.7%), amikacin (11.2%), vancomycin (9%), and ciprofloxacin (8.9%). A recent study carried out in Ethiopia exhibited that ceftriaxone, based on its high potency, is a common antibiotic, and its inappropriate use has been led to bacterial resistance in this country (27). Also, incorrect use of vancomycin, meropenem, and ciprofloxacin is demonstrated in other studies as a big problem (28-30). Moreover, our study compared the prescribed antibiotics for some microorganisms according to the suggested antibiotics in the clinical course books including Harrison's infectious diseases (31), Mandell, Douglas Bennett's Principles

Practice of Infectious Diseases (18), and in a laboratory coursebook, the Clinical & Laboratory Standards Institute (*CLSI*) guidelines (32).

Another point about the present study is that some of the microorganisms in our research were resistant to some antibiotics which Harrison's book has been approved for the treatment of the infections caused by those microorganisms. For example, ceftriaxone is approved for the treatment of the infections caused by coagulase-negative staphylococci in this book, and even the physicians prescribed it in our region, but these organisms were resistant against this antibiotic based on the laboratory antimicrobial susceptibility testing (AST). Maybe these microorganisms in our area have been resistant to ceftriaxone due to the misuse or overuse of this antibiotic in our hospitals. Also, according to the Harrison book, E. coli is known as resistant microorganism to ampicillin and amoxicillin, but in laboratory tests, the bacteria is sensitive, and the physicians have no problem in prescription. Another view is that we have many cases that the physicians prescribed the antibiotics correctly, moreover, the laboratory tests and course books approved them, too. For instance, there is no misuse of the prescription for S. pneumonia and Acinetobacter spp. According to the course books and the laboratory tests, they were indicating that bacterial resistance is not happening about these infections.

Another problem in our data was that 28 cases in which the laboratory tests detected bacterial infections in samples, but physicians didn't prescribe any antibiotics for them. On the other hand, our findings indicated that the most antibiotics prescribed for the treatment of the bacterial infections of the patients in the present study were common broad-spectrum antibiotics. We had 110 cases that physicians prescribed three different classes of antibiotics, 49 cases with four different antibiotics, and 7 cases with five different classes of antibiotics. In general, the most common prescription was contained two different antibiotics, and this process was tended to decrease for more antibiotics. This type of prescription could be related to the emergence of bacterial resistance (33). The physicians' prescriptions based on their experience without considering the AST, along with the use of several classes of the antibiotics, may amplify this problem.

We found many cases that physicians falsely prescribed antibiotics according to the laboratory AST (Table 3). This shows that maybe physicians didn't rely on laboratory tests, or they believed these antibiotics have a good response in clinical based on their experience. This inappropriate antibiotic usage can cause the emergence of resistance in other microorganisms (34). Then, the educational programs, consultation by infectious physicians, timely narrowing of broad-spectrum empirical

therapy, and stop automatic orders are necessary to antibiotic management and the prevention of the bacterial antibiotic resistance in the hospitals (35).

Conclusions

Inappropriate use of antibiotics was widely seen. This value may, in the future, lead to antibiotic resistance and therefore, the need for more powerful antibiotics with greater side effects. The prescription of antibiotics without looking at laboratory tests may amplify this problem. There seems to be a need to set up a team to prevent this and to pay attention to the antibiotics prescribed for infectious patients. These include training programs for physicians, consulting with infectious disease specialists, reducing empirical prescriptions by physicians, and spontaneous antibiotic use by patients.

Conflict of interest

The authors declare no conflict of interest.

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