The Characteristics of Antibiotic Use and Changing Patterns in an Intensive Care Unit

Yoğun Bakım Ünitesinde Antibiyotik Kullanım ve Değişim Özellikleri

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Abstract

Objective: Infections are frequently seen in critically-ill patients and they are associated with increased mortality, morbidity and cost. Antibiotics play a very important role in the prevention and treatment of infections, yet associated with increased resistance especially when used inappropriately. In our study, we analyzed the data regarding antibiotic use before and during intensive care and we evaluated factors related to antibiotic change.

Material and Methods: The study was conducted in a medical intensive care unit (ICU) of a university hospital. Adult patients, who were admitted to the ICU and were using antibiotics in a 1 year-period, were included in the retrospective analysis.

Results: One hundred and seventy-six patients were included in the study. 58% of patients (n=103) were male. Mean (± standard deviation) age was 60.9±18.0 years. The percentage of patients who were referred to ICU from emergency room was 73%, while 23% of the patients were referred from inpatient services and 4% of the patients from another hospital. In 83% (n=146) of the patients, antibiotics were started before ICU admission. The primary reason for initiation of antibiotic therapy was recorded as pneumonia in 57% of the patients. Antibiotics were changed in 39% (n=69) of patients upon admission to ICU and in 68% (n=120) of patients during ICU stay. The sequential organ failure assessment (SOFA) score on the day of antibiotic change was higher than the SOFA score on ICU admission (p=0.001).

Conclusion: Antibiotic change is highly made in critically ill patients. Mostly patients use antibiotic before ICU admission. SOFA score can be used for antibiotic change decision.

Keywords: Critically ill, infection, antibiotic, intensive care unit

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Öz

Amaç: İnfeksiyonlar yoğun bakım (YBÜ) hastalarında sıklıkla görülür ve artmış mortalite morbidite ve maliyetle ilişkilidir. Antibiyotikler infeksiyonların tedavisi ve önlenmesinde önemli rol almalarına rağmen özellikle uygunsuz kullanımda direnç artımı ile ilişkilendirilirler. Bu çalışmada, yoğun bakım öncesi ve esnasında antibiyotik kullanımını analiz ettik ve antibiyotik değişimi ile ilgili faktörleri değerlendirdik.

Gereç ve Yöntemler: Çalışma bir üniversite hastanesi erişkin medikal yoğun bakım ünitesinde yapıldı. Çalışmaya 1 yıllık periyotta yoğun bakıma yatan ve antibiyotik kullanan erişkinler dahil edildi ve retrospektif olarak analiz edildi.

Bulgular: Çalışmaya 176 hasta dahil edildi. Hastaların %58'i (n=103) erkekti. Ortalama (± standart sapma) yaş 60,9±18,0 idi. YBÜ'ye alınan hastaların %72,7'si acil servisten gelirken %23,3'ü yatan hasta servislerinden ve %4'ü başka bir hastaneden gelmişti. Hastaların %83'üne (n=146) yoğun bakım öncesi antibiyotik başlanmıştı. Antibiyotik başlanmasının birincil nedeni %56,8 ile pnömoniydi. YBÜ gelişte %39,2 (n=69) oranında ve YBÜ yatışı esnasında %68,2 (n=120) oranında antibiyotik değiştirilmişti. Antibiyotik değişim günü Sequential Organ Failure Assessment skoru (SOFA) YBÜ yatış günü SOFA skorundan yüksekti (p=0,001).

Sonuç: Yoğun Bakım hastalarında yüksek oranda antibiyotik değişimi yapılmaktadır. Hastaların çoğu yoğun bakım öncesi antibiyotik kullanmaktadır. Antibiyotik değişim kararında SOFA skoru değerlendirilebilir.

Anahtar Kelimeler: Kritik hasta, enfeksiyon, antibiyotik, yoğun bakım ünitesi

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Introduction

Infections are frequent problems in critically-ill patients and they are associated with increased mortality, morbidity and cost (1-4). Compared to the other hospitalized patients, presence of concomitant co-morbidities, severe acute physiological disorders, relative immunosuppression and frequent invasive procedures are the most common risk factors for acquisition of infections in the critically-ill patients who generally receive longer and various kinds of antibiotics (5, 6). These factors lead to emergence of multi-drug-resistant microorganisms in intensive care units (ICU) (7, 8) and since treatment of resistant microorganisms is difficult, this problem results in increased mortality, morbidity and costs (9, 10).

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Development of resistance is related with antibiotic use. Therefore, antibiotic prescription strategies before and during ICU stay are crucial. In this study, we investigated the frequency of antibiotic use before ICU admission, the frequency of antibiotic changes, and we evaluated the factors related to antibiotic change.

Material and Methods

The study was conducted in Medical Intensive Care Unit of a university hospital. Adult patients, who were admitted to ICU between January 1st, 2013 and January 1st, 2014, who stayed for more than 48 hours and were using antibiotics, were included in the study. Data were collected retrospectively from the patient files and hospital database.

Age, gender, Acute Physiology and Chronic Health Evaluation Score (APACHE II), Sequential Organ Failure Assessment (SOFA) score, C-reactive protein (CRP) and procalcitonin (PCT) values, place before ICU admission, the primary reason for the antibiotic initiation, place where the first culture was taken, duration of hospitalization and antibiotic use before ICU admission, the number and reason of antibiotic changes during ICU stay, , isolated microorganisms, sites of infection, total duration of antibiotic use and duration of hospitalization were recorded.

Ethical committee approval was obtained prior to the study (GO 14/191-29, 19.03.2014)

Statistical analysis

Analysis was performed using SPSS version 21.0.0.1 (SPSS, IBM, Armonk, NY, USA). The descriptive statistical method was used for demographic data. Wilcoxon test was used for the analysis of ordered variables. Pearson correlation test was used to assess the correlation between numerical variables. Results are presented as mean ± standard deviation or median (minimum-maximum). A p value <0.05 was considered as statistically significant.

Results

A total of 176 patients were included in the study. The mean ± standard deviation (SD) age of patients was 60.9±18.0 years. The number of male patients was 103 (58%). The descriptive and demographic information of patients are shown in Table 1. The patients were mostly transferred to ICU from emergency department (73%). Acute respiratory failure was the first reason for ICU admission (67%) (Table 1).

Antibiotics were started prior to ICU admission in 83% (n=146) of the patients. The median (minimum-maximum) duration of antibiotic use before ICU was 2 (0-59) days. Total duration of antibiotic use was 17.5 (1-116) days. The most common reason for antibiotic initiation was pneumonia (57%). Cultures were taken from at least one site in 75% patients prior to antibiotic treatment (Table 2). As shown in Table 2, in 39% of the patients, antibiotics were changed at ICU admission. The most common isolated microorganism was *Acinetobacter baumannii* (24%). The most common infection site was respiratory system (35%) and quantitative deep tracheal aspirate was the most frequent (35%) culture method.

SOFA score was higher on antibiotic change day compared to the score calculated on ICU admission day (p=0.001, Table 3). The relationships between SOFA, CRP and Procalcitonin values in ICU admission day and antibiotic change day are shown in Table 4. There was weak, yet significant, correlation between SOFA-CRP, SOFA-Procalcitonin and CRP-Procalcitonin values (Table 4).

The median lengths of ICU and hospital stay were 9.5 (1-72) and 23 (5-184), respectively. ICU mortality was 31.8% and hospital mortality was 42.6%.

Table 1. The descriptive and demographic data of patients

Characteristics	**n=176**
Age, mean±SD	60.9±18.0
Male	103 (32)
APACHE II, mean±SD	18.6±7.8
SOFA at admission, mean±SD	5.6±2.6
Place before ICU admission n (%)	
Emergency room	128 (72.7)
Inpatient service	41 (23.3)
Other hospital	7 (4)
Reason for ICU admission n (%)	
Acute respiratory failure	119 (67)
Sepsis	52 (29)
Other	25 (14)
Co-morbidities n (%)[a]	
Hypertension	76 (43)
Chronic pulmonary disease	69 (39)
Congestive heart failure	61 (34)
Cancer	48 (27)
Diabetes mellitus	35 (20)
Renal disease	30 (17)

[a] Total is not equal 100%, since some patients have more than one comorbidity.
APACHE II: Acute Physiology and Chronic Health Evaluation Score;
SOFA: Sequential organ failure assessment; ICU: intensive care unit; SD: standard deviation

Discussion

In this study, we evaluated the antibiotic use in ICU. We showed that the vast majority of critically ill patients were exposed to antibiotics before ICU admission. Antibiotics were changed at ICU admission in significant number of patients. In addition, we found that SOFA score was higher on antibiotic change day.

One of the major causes of increased resistance is antibiotic use prior to intensive care admission (11). In a prospective observational study in 41 French ICUs, Montravers et al. (12) found that 28% patients already were administered antibiotic therapy before ICU admission. In contrast, in our study, 83% of patients had already been using antibiotics before ICU admission. In our study, in 75% of patients, cultures were obtained prior to antibiotic therapy. However, we have inadequate data about the adequacy and appropriateness of culture sites since in majority of patients only blood cultures were taken.

Extended Prevalence and Epidemiology of Infection in Critically-ill (EPIC) study (13), in which the prevalence and outcome of ICU acquired infections were investigated, showed that the most common site of infection was lungs with a frequency of 64%, similar to our study where the most frequent site being lungs with a frequency of 67%. In the EPIC II study, the culture-positivity was 70% similar to our study in which frequency of positive cultures was 66%. The most common isolated microorganism in our study was *Acinetobacter baumannii* with a frequency of 23.8%. In the EPIC II study, prevalence of *Acinetobacter infection* differed widely according to geographical regions. It was found to be 3.7% in North America where as 20% in Asia with an average prevalence rate of 9% (13).

Table 2. The data regarding antibiotic use, isolated microorganisms and culture sites

	n (%)
Reason for antibiotic initiation before intensive care	
Pneumonia	100 (56.8)
COPD exacerbation	19 (10.8)
Sepsis	15 (8.6)
Other	42 (23.8)
Taking cultures prior to antibiotic treatment	132 (75)
Antibiotic change at admission to ICU	69 (39.2)
Frequency of antibiotic change during ICU stay	120 (68.2)
1	74
2	23
>3	23
Frequency of positive cultures during ICU stay	107 (60.8)
Isolated microorganisms [a]	
Acinetobacter baumannii	42 (23.8)
Klebsiella pneumonia	20 (11.3)
Escherichia coli	19 (10.7)
Enterococcus spp	17 (9.6)
Pseudomanas aeruginosa	16 (9)
Staphylococcus aureus	5 (2.8)
Mycobacterium tuberculosis	5 (2.8)
Polymicrobial microorganisms	47 (26.7)
Other microorganisms	36 (20.4)
Culture sites [a]	
Quantitative deep tracheal aspirate	62 (35.2)
Blood	41 (23.3)
Intravascular catheter	33 (18.8)
Urine	31 (17.6)
Others	28 (15.9)
More than one site	55 (31.3)

[a]Total is not equal to 100% since some patients have been infected with more than one type of microorganism from different sites.
COPD: Chronic obstructive pulmonary disease; ICU: intensive care unit

Table 3. SOFA score and infection biomarkers at ICU admission day and at antibiotic change day

	ICU admission day	Antibiotic change day	p
SOFA	5.6 (±2.6)	6.5 (±6.5)	0.001
Procalcitonin	7.3 (±27.6)	10.3 (± 35.9)	0.599
CRP	11.6 (±10.6)	11.3 (±9.6)	0.609

SOFA: Sequential organ failure assessment; CRP: C-reactive protein

In our study, antibiotic changing rate is 39% probably because of better evaluation of patients in the ICU and because critically-ill patients might have more complicated infections with different antibiotic susceptibility profiles. Nevertheless, using different antibiotics can cause more resistant infections (11).

Table 4. Correlation of infection biomarkers and SOFA score in antibiotic change day

	r	p
Procalcitonin and CRP (n=87)	0.450	<0.001
Procalcitonin and SOFA (n=91)	0.481	<0.001
CRP and SOFA (n=91)	0.322	0.002

SOFA: Sequential organ failure assessment; CRP: C-reactive protein

SOFA score is developed to evaluate the degree and severity of organ failures, generally used to track a patient's status during the stay in ICU (14-16). Several studies have shown that SOFA score can be used to predict short- and long-term mortality (14, 17, 18). In our study, we found that there was a statistically significant difference between the SOFA score on ICU admission day and the score on the day when antibiotic was changed. Therefore, an increase in SOFA score might be a warning sign for acquisition of new infection or new microorganism with a different antibiotic susceptibility profile.

The markers such as CRP and PCT are used as surrogate markers in diagnosis and follow-up of infections. Several studies revealed that PCT had greater diagnostic accuracy than CRP, IL-6, IL-8 to distinguish between bacterial sepsis and non-infectious etiologies of systemic inflammatory response syndrome (SIRS) (19-21). In contrast, some other studies have shown greater utility of CRP than PCT (22, 23). The debate of biomarker guided antibiotic therapy is ongoing. Two-center randomized controlled trial demonstrated that measuring daily PCT and using PCT guidance for antibiotic initiation and withholding resulted in a decrease in overall antibiotic use from 15 to 10 days in 101 patients with ventilator associated pneumonia (VAP) (24). In a French study (25) on non-surgical patients with suspected bacterial infection (73% with a respiratory infection) in seven ICUs, PCT-guided treatment initiation and discontinuation provided 23% more antibiotic free days compared to the control group (25). On the other hand, in a RCT in two Brazilian ICUs, a CRP-based algorithm was compared to a PCT-based algorithm in patients with severe sepsis and septic shock and CRP-based algorithm was found to have similar success (26). In our study, we observed that there is a moderate correlation between PCT versus SOFA and CRP versus SOFA at the antibiotic change day. Unfortunately, PCT and CRP had not been performed in all patients.

Antibiotic duration is another factor related with development of resistance. Therefore, antibiotic duration has been progressively shortened for many infectious syndromes (27). Current recommendations for duration of antibiotics for community-acquired pneumonia are about 7 days (28), for pyelonephritis 5-7 days (29) and VAP 8 days (30). In our study, median antibiotic use before ICU admission was 2 days (min-max 0-59) and the overall median antibiotic use during intensive care stay was as long as 17 days (2-116). Reasons for using antibiotics for a long duration are as follows: First, there is not a formal antibiotic stewardship program in our hospital. Increased resistance rates mandate that all ICUs should incorporate an antibiotic stewardship program with a multidisciplinary approach to decrease resistance and improve outcome (31). Secondly, using more antibiotics before ICU admission leads to acquisition of more resistant microorganisms, which leads to longer treatment duration. Third, we do not have a formal algorithm for antibiotic initiation, de-escalation or withholding. And the last but not the least, intensivists in Turkey have minimal roles in antibiotic prescriptions due to legal restraints, which need to be reviewed.

Our study has some limitations. It is a retrospective study. Furthermore, we could not assess whether cultures were obtained from ap-

propriate sites especially before ICU admission. We were not be able to present information about timing and appropriateness of empirical antibiotic treatment, as well. PCT and CRP measurements were not performed in antibiotic changing day, in all patients. Finally, we could not determine the exact causes of antibiotic changes.

Conclusion

Antibiotic consumption especially prior to ICU admission is very high in critically ill patients. SOFA score might be used as a warning score for decision of antibiotic change.

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