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Research Article

A Study to Evaluate Appropriateness of Empirical Antibiotic Use in Intensive Care Unit of King Saud Medical City, Riyadh, Saudi Arabia

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ABSTRACT

Background: Antibiotics are commonly administered therapies in ICU. There has been a concern over antibiotic misuse recently. ICU is both a victim and a contributor to the ongoing antibiotic misuse problem and a cause of emerging resistance among the pathogens commonly acquired in intensive care units. Because of high mortality associated with sepsis, it is a great challenge for intensive care physicians to select appropriate antibiotic sometimes without any culture and sensitivity. Similarly the time to deescalate also remains a tough call. Selection of appropriate antibiotics empirically has always been a topic of debate among Intensive Care and Infectious Disease practitioners.

Objective: The aim of our pilot study was not only to assess the appropriateness of use of antibiotics in our ICU but to help us guide to design a bigger study and structure a stewardship program for ICU. Also to assess the differences among prescription of ICU and Infectious Disease Consultants.

Methods: A prospective observational study in King Saud Medical City ICU following antibiotics started and stopped from 6th November 2014 to 23rd November 2014. Study included 23 adult patients admitted with different etiologies. All 23 patients' records were shared with two alien referees (one was infectious diseases and other was ICU consultant) from other hospital. Prescribers were blinded to the fact that data was being collected for auditing and the referees were blinded to prescribers and to each other's.

Results: Total 46 antibiotics were used. 40 among them were started on empirically, 6 were culture based. 31 antibiotics were stopped by ICU. 28 among these 31 antibiotics were empirical. Most of included patients responded to combination or monotherapy. Piperacillin-Tazobactam was the most commonly prescribed antibiotic. No major difference was noted among the choice of intensive care or infectious disease consultant.

Conclusion: Empirical antibiotics are vital for patients admitted in ICU. We need to follow hospital's anti-biogram and stewardship programs with prompt de-escalation wherever appropriate.

Keywords: Empirical antimicrobial therapy; Culture and sensitivity; Antibiotics; De-escalation; Antibiotics stewardship; Antimicrobial guidelines

INTRODUCTION

Selection of antibiotics in the era of high resistance and lack of new antimicrobial development in intensive care settings is crucial [1,2]. Appropriate administration of antibiotics is major determinant for the outcomes in case of severe bacterial infections in intensive care (ICU) settings [3]. To avoid unnecessary antibiotic administration and increase therapeutic effectiveness usually locally accepted or national society based guideline or protocols are followed. Even well-developed guidelines or protocols may not translate into widely accepted treatment algorithms. Some deviation from guidelines and protocols is expected as medical decision making is usually guided by individual patient's characteristics and the judgment and experience of the caregivers [4].

Antimicrobials are the major drugs used in intensive care units (ICU), although their undiscriminating and prolonged use is one of the main factors involved in the emergence of multidrug-resistant bacteria, whose incidence has grown in all continents [5]. Typical clinical signs of infection, such as fever or raised white

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blood cell count, are non-specific and can occur in many other conditions in the critically ill population. Similarly, although many biomarkers, e.g., C-reactive protein and Procalcitonin (PCT) [6], have been suggested to help diagnosis or to rule out infection, none is specific for infection and all can be altered in other conditions that commonly affect ICU patients. Diagnosis of infection still relies largely on culture-based techniques, which can take several days for a positive result to be available.

Moreover, in patients already receiving antibiotics, cultures may be negative [7]. The ICU is considered among most important sources of nosocomial infections [8]. The high prevalence of infections involves heavy consumption of antimicrobial agents which is 10 times more than in general wards [9]. In all these circumstances, actual implementation of antimicrobial therapy (AMT) prescription guideline or antibiotics stewardship is needed. However, it does not provide insight into the appropriateness of antimicrobial therapy and about determinants of inappropriate use [10].

We design this study proposal to determine the appropriateness of empirical antibiotics prescription in an intensive care unit.

PATIENTS AND METHODS

Study was conducted in King Saud Medical City, Riyadh KSA from 6th November 2014 to 23rd November 2014. Total 26 patients of adult age from 18-90 years, and those who were started on antibiotics within first week of admission in ICU were included in study. All those below 18 years, patients with ICU stay<24 hrs, and those with DNR (Do not resuscitate) status were excluded from study. Data like age, gender, White cell count, C-Reactive Protein), Serum Lactate levels, Chest X-Rays, Cultures and Sensitivities, type of antibiotics, start of antibiotics, duration in ICU, discontinuation of antibiotics was collected. 3 patients did not completed follow-up, so they were excluded from study as well.

Study started after ethical committee's approval. Informed consents were taken. All data was also presented to alien referees to give detailed comments.

Statistical analysis

We performed prospective observational study. Statistical analysis performed by using IBM SPSS version 20.0. Type of antibiotics represented in percentages. P-value<0.05 is considered significant. Use of antibiotics, mentioned in frequency tables.

RESULTS

In this study we included 26 patients, 3 patients were excluded from study, as they did not complete follow up. Median age was 48 years, for 18-90 years of age. In our study 12 males and 11 females were included. Total 46 antibiotics were started for 23 patients. Among them 40 antibiotics were started on empirical basis with significant P-value. Only 6 antibiotics were started based on cultures (Table 1). In relation to these antibiotics about their stoppage, 7 patients died in ICU, 8 patients were discharged on antibiotics from ICU to general ward. We found that 31 out of 46 antibiotics were discontinued in ICU. P-value was significant for this group of antibiotics as it was <0.05. The duration of these 31 antibiotics was 2-15 days, with median duration of 6 days. This indicates that antibiotics provided appropriate cover and most of the antibiotics among them were based on empirical therapy in 28 out of the 31 patients. Only 3 were started based on available cultures (Table 1).

Table 1: Demographic characteristics of patients.

Characteristics of patients	Total Numbers	p-value
No of patients	26	-
Age	18-90 yr (48 yrs Median)	-
Gender		
Male	12	-
Female	11	-
No and types Of antibiotics started	46	-
Antibiotic started on empirical bases	40	<0.001
Antibiotics started based on cultures	6	-
Pt died in ICU	7	-
Pt discharged on antibiotics from ICU	8	-
Total antibiotic discontinued in ICU	31	<0.03
Out of total 31 antibiotics stopped in ICU, started empirically	28	<0.01
Out of total 6 antibiotics stopped in ICU, started on culture base	3	-
Duration of 31 antibiotics in ICU	2-15 days (6days Median)	6 days

As far as, detailed number of antibiotics is concerned. Only one (17.39%) antibiotic was started in 8 patients (34.7%). Among 9 patients (39.1%), 2 antibiotics were started. So, maximum percentages of patients were prescribed 2 antibiotics. However, 4 (17.39%) patients required 3 (26%) antibiotics for their infection to be treated. Maximum 4 antibiotics were started in 2 out of the 23 patients (17.39%) (Table 2).

Table 2: Details of antimicrobial therapy.

No. of patients	No. of antibiotics started	% Age
8/23 (34.7%)	1	17.39%
9/23 (39.1%	2	39.10%
4/23 (17.39%)	3	26.00%
2/23 (8.6%)	4	17.39%
Monotherapy started	23-Aug	17.39%
combination therapy	15/23	82.49%
Type of antibiotics started		
Piperacillin-tazobactam	14	30.40%
Macrolides	9	19.60%
Carbapenem	6	13%
Third generation cephalosporin	5	10.90%
Vancomycin and linezolid	3	6.50%
Sulfamethoxazole and trimethoprim	1	2.20%

The most commonly used antibiotics in our study were Piperacillin-Tazobactam 30.4% it was used on 14 patients along with other antibiotics. Macrolides were used in 9 (19.6%) individuals. Carbapenems and 3rd generation Cephalosporins were used in 6 (13%) and 5 (10.9%) patients respectively. Vancomycin and Linezolid were prescribed 3 times (6.5%) respectively. However, Sulfamethoxazole and trimethoprim was used in 1 (2.2%) patient.

Referees comments

The ID (Infectious diseases consultant) referee agreed antibiotics were needed in 82.6% of cases while the Intensivist (ICU Consultant) agreed with 95.5%. Most cases (63% in ID's opinion and 66.7% in intensivist's) did not need source control. In some cases (15.2% for ID and 17.8% for intensivist) data was not sufficient to decide. ID consultant thought 9 cases needed source control of which 6 were adequate. Intensivist said only 6 needed source control of which only 3 were adequate.

Empirical antibiotics were 71.7% appropriate and 19.6% inappropriate (the rest were either C/S based or he couldn't decide) from ID point of view while 73.3% were appropriate and 15.6% inappropriate from Intensivist's point of view. Collecting cultures were adequate in 80.4% of cases judged by ID consultant but only 62.2% adequate for the intensivist. De-escalation was not needed for most cases (76.1% & 77.8% respectively).

Appropriate de-escalation took place in 7 out of 11 cases judged by ID and in 8 out of 9 judged by intensivist Modification in antibiotics with time was not needed in 63% and 44.4% of cases respectively for ID and ICU Referees. It was needed for 13 antibiotics of which 9 were appropriately modified judged by ID Consultant and was done appropriately for 14 out of 18 as judged by intensivist. Dose was judged to be appropriate only 65.2% of the time by ID and only 82.2% of the time by Intensivist. ID consultant couldn't comment on duration in 32.6% of cases. To him it was appropriate in 47.8% and inappropriate (too short or too long) in 19.6%. Referee Intensivist couldn't comment on 46.7% of cases. To him it was appropriate in 44.4% and inappropriate only in 6.7% of cases.

Overall antibiotic courses without any inappropriate aspect were 19/46 (41.3%) for both the ID consultant and the consultant intensivist independently.

DISCUSSION

Empirical treatment should be based on regularly updated data on trends of incidence and susceptibility to antimicrobial agents in a particular setting [11]. Through the initiation of active empiric antibiotic therapy based upon local susceptibilities, daily evaluation of signs and symptoms of infection and narrowing of antibiotic therapy when feasible, providers can streamline the treatment of common intensive care unit (ICU) infections [12]. 40 Empirical antibiotic started in ICU in our study with significant P-value<0.00 Michael and colleague identified that estimates of the potential benefit of appropriate empirical antibiotic treatment vary widely in the literature [13]. Garnacho and colleagues [14] identified that De-escalation of antibiotics in ICU ranges from 10%-60% in critically ill patients. De-escalation refers to stoppage of antibiotic or switching to other agent with narrow spectrum. Among empirical therapy, we stopped 28 out of 31 antibiotics in our study in ICU with significant P-value and only 8/31 were discharged from ICU with antibiotics. In our study around 82% patients (15/23) were started with combination therapy as compare to monotherapy e.g., 17.1%. Similar results were seen in one study. Pierre [15] suggested that combination therapy mainly benefits the most severely ill patients and bacteremia patients.

Jose and colleagues [16] noted the most common initial antibiotics which were prescribed were Cefoperazone-Sulbactum or Piperacillin-Tazobactum. Our study also revealed similar pattern in choice of antibiotic used e.g., maximum patients were given Piperacillin-Tazobactam, Macrolides and Carbapenem.

Still there is no single recognized policy to identify about which antibiotic should be used at proper time, Consequently, antibiotic prescribing remains far from the guidelines, probably because intensive care physicians are receptive to different advice [17]. These circumstances urgently call for high-quality evidence in this field and further stress the importance of establishing local and national surveillance systems, as well as the development of multi-disciplinary approaches to antibiotic management and guideline production. By adopting these guidelines common censuses can be adopted on wide range in order to streamline the antibiotics usage in intensive care settings.

CONCLUSION

Empiric antibiotics selection is a major undertaking on part of ICU physicians as it plays an important role in outcome of critically sick patients. No major difference was noted among the choice of intensive care or infectious disease consultant

Referees are neither superior nor inferior to prescribers (ICU physicians in our study) but they had the privilege of looking retrospectively at the cases when things had become clearer.

They also were privileged to be away from the heat of the bedside situation, peer pressure, pressure from families of patients and medicolegal responsibility. We believe that this pilot will be of great help in designing a bigger prospective study. We understand that the sample was not powered enough to detect any statistically significant findings. The percentage of overall appropriateness is consistent with previously published bigger studies. It seems that our empirical choices were appropriate most of the time but our weakest points come from collection of proper cultures then de-escalation/modification according to clinical and bacteriological data.

CONFLICT OF INTEREST

The authors have declared no conflict of interests.

DATA AVAILABILITY STATEMENT

This was an observational study and data is safe and available in KSMC.

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