Antibiotic prescribing pattern in a Medical Intensive Care Unit in Qatar

Yolande Hanssens, *MESCP, FASCPT,* ***Bassam B. Ismaeil,*** *MBChB, MMed-path (MedMicro),* ***Ahmed A. Kamha,*** *MRCP, CABMS,* ***Sittana S. Elshafie,*** *MSc, FRCPath,* ***Fathia S. Adheir,*** *BPharm,* ***Thoraya M. Saleh,*** *MSc, MRCPath(1),* ***Dirk Deleu,*** *FAAN, FRCP.*

ABSTRACT

Objectives: The primary objectives were to evaluate the current usage of anti-microbial agents in the Medical Intensive Care Unit (MICU) of Hamad Medical Corporation (HMC) in Doha, State of Qatar and to correlate this with: a) the infectious disease pattern, b) the isolated microorganisms and their sensitivity pattern, and, importantly, c) the patient's clinical outcome. A secondary objective was to evaluate the influence of the use of steroid therapy on the development of fungal infections.

Methods: A prospective study covering a 2-month period from February through April 2004, including all patients admitted to the MICU for a minimum of 48 hours, and receiving a systemic antibiotic.

Results: From the 71 eligible patients admitted, 54 (76%) were treated for presumed or proven infections and received antibiotics, corresponding with 280 (89%) of the 313 patient days. Respiratory infections accounted for 57%. A total of 159 antibiotics (134 intravenously and 25 orally) were administered to the 54 patients during their stay in the MICU, corresponding with an average of almost 3 antibiotics per patient. Ceftriaxone was prescribed in 31 patients (57%) as initial therapy. Throughout the study period, a total of 385 microbiology samples for culturing were taken, corresponding with almost one sample per patient per day. Fifty-two percent of patients had a microbiologically proven infection (MPI): 18% with community-acquired pneumonia (CAP), 18% ventilated-acquired pneumonia (VAP), and 11% with hospital-acquired pneumonia (HAP). In the group of bacterial MPI, sensitivity pattern resulted in change in empirical antibiotic therapy in 12 of 23 patients (52%). In the group of patients with non-MPI, antibiotherapy was changed in 5 of the 26 patients (19%). Yeast infections developed in 13 of 30 (43%) patients receiving steroids (with 3 out of 9 patients (33%) receiving steroids for severe sepsis, and septic shock) compared to 5 of 24 (21%) patients receiving no steroids.

Conclusion: This study highlights the urgent need for updated empiric and treatment guidelines as well as the monitoring of the antibiotic usage.

Saudi Med J 2005; Vol. 26 (8): 1269-1276

Antibiotics are widely used in intensive care units.[1] Large medical intensive care units (MICU) with a varied case mix are more vulnerable to infection control problems compared to smaller units caring mainly for postoperative patients.[2] The characteristics of careful antibiotic usage are simple: when an infection is clinically suspected, samples for microbiological cultures should be obtained before starting empiric therapy.[3] Adequacy of initial empirical antimicrobial treatment is crucial in terms of outcome. The immunocompetence of the patient, it should be individualized virulence of suspected microorganisms and antibiotic related issues (for example, possible contraindications, adverse

From the Clinical Pharmacy Services, Pharmacy Department (Hanssens, Adheir), Microbiology (Ismaeil, Elshafie, Saleh), Medical Intensive Care Unit (Kamha), and Neurology (Deleu), Hamad Medical Corporation, Doha, *State of Qatar*.

Received 1st March 2005. Accepted for publication in final form 17th May 2005.

Address correspondence and reprint request to: Dr. Yolande Hanssens, Pharmacy Department, Hamad Medical Corporation, PO Box 3050, Doha *State of Qatar*. Tel. +974 4392186. Fax. +974 4392253. E-mail: yhanssens@hmc.org.qa.

reactions, interactions) taken into account. Based on culture results as well as clinical signs and symptoms, empiric therapy can be continued, adjusted or discontinued. In clinical practice, however, usage of antibiotics is often continued despite negative culture results. The patient's condition is often judged as too serious, and too critical to withhold further antibiotic treatment.[3] In 2003, 935 patients were admitted to this MICU with 257 patients admitted during the first 3 months of 2003. This figure correlated very well with the number of patients admitted in the first trimester of 2004, being 255. Patients are admitted from medical units and through the emergency department. In 2003, the mortality rate reached 17.8%. The overall disease pattern involves renal failure (15-18%), followed by gastrointestinal bleeding (10-12%). The current antibiotic policy in Hamad Medical Corporation (HMC) divides the antibiotics into 3 lists: unrestricted list, which includes drugs that can be prescribed by all categories of doctors on an in- and outpatient basis.[4] Besides the very basic antibiotics, such as amoxicillin, cefuroxime (oral only), and erythromycin, surprisingly, this list also includes gentamicin, and anti-TB drugs. The second group of antibiotics (restricted list I) lists mainly second-line drugs, such as amoxi-clav, azithromycin (oral), and cefepime. These can only be prescribed by consultants, and specialists after culture and sensitivity results become available. The third group (restricted list II) is a total of 12 more specialized (more toxic, broader spectrum, or higher cost, or both) antibiotics, such as amikacin, meropenem and vancomycin, and can only be prescribed by consultants and specialists from the infectious disease team. Exceptions are made for immunocompromised patients, and patients in all intensive care units where all consultants and specialists are entitled to prescribe these drugs empirically for a maximum of 48 hours. Subsequently, results of cultures as well as sensitivity testing should provide further guidance for continued treatment. Since no updated hospital antibiotic guidelines are available, empirical antibiotic (EAB) therapy is mainly based on experience (for example all community-acquired pneumonias receive ceftriaxone and azithromycin), and international guidelines. The use of steroids in the management of patients with severe sepsis, and septic shock remains one of the most controversial clinical issues in critical care,[5-7] and should probably be reserved for a select subset of patients, steroid substitution therapy is routinely used in this MICU.[8] Drug use review (DUR) and evaluation of prescribing patterns are common in Western countries, but is relatively a new concept in the Arabian Gulf countries. The primary objectives of this DUR were to evaluate the current usage of anti-microbial agents in MICU at HMC, and to correlate this with: a) the infectious disease pattern, b) the isolated microorganisms and their sensitivity pattern, and, importantly, c) the patient's clinical outcome. A secondary objective was to the influence of the use of steroid therapy on the development of fungal infections was also evaluated. The findings of this DUR could potentially result in a modification of the current antibiotic policy, and could serve as a template for DURs in other units.

Methods. Hamad Medical Corporation at Doha, State of Qatar, is a tertiary referral center with a total capacity of 1,600 beds covering all medical, and surgical disciplines including 6 intensive care units for adults. The patient population includes locals as well as expatriates mainly from other Arab countries and Asia.[4] The MICU at HMC has 17 beds; 13 acute care beds, and 4 step down beds. This DUR was performed in the MICU of HMC, which is managed by one consultant, 2 specialists, and 3 residents. The MICU also serves as a unit for residents rotating in internal medicine, and emergency medicine. Furthermore, weekend and evening on-call duties are cared for by a specialist from the MICU team. Finally, where deemed essential, consultants from all disciplines are called in and the infectious disease team is involved at least for patients receiving more than 2 antibiotics. On admission, the MICU standard protocol at HMC comprises a complete septic work-up when the patient has fever. This includes testing for human immunodeficiency virus (HIV), Hepatitis B and C. Clinical findings, microbiological results, and antibiotic therapy can be discussed with the infectious disease, and medical microbiology team. Recently, a clinical pharmacist joined the MICU team during its daily rounds, and initiated this DUR in collaboration with the consultant of MICU, and the medical microbiology team. The MICU consultant completed the clinical data, and the medical microbiologists provided culture and sensitivity patterns. The clinical pharmacist performed data collection at the time of discharge of the patient from MICU, and included the microbiological data as they became available. To keep the DUR as objective as possible, the clinical pharmacist did not interfere with the EAB therapy. However, in patients with unjustified initiation of EAB therapy, the prescription was challenged.

During a 2-month period (February through April 2004), all patients admitted to MICU were prospectively evaluated. All patients admitted for a minimum of 48 hours, and receiving a systemic antibiotic were included. The following data were recorded: gender, age, nationality, medical history, current diagnosis (for example suspected site of infection), temperature, white blood cell count, admission status (directly through the emergency

department or transferred from a hospital ward), antibiotic usage before admission to MICU, length of stay (LOS) in MICU, interventions (including central line and mechanical ventilation), co-morbid conditions, mortality in MICU, the usage of corticosteroids, collection of samples for microbiological cultures on admission and during the stay at MICU, microbiological results (including sensitivity patterns), antibiotic usage in MICU (including drug and reason for its use). The reason for any discontinuation of antibiotic therapy was recorded. Depending on microbiological results, infections were categorized into 2 categories: microbiologically proven infections (MPI) and non-microbiologically proven infections (non-MPI). The MPI were defined as an infection for which a serology or a positive culture resulting from samples collected at a suspected site of infection was obtained. Non-MPI was defined as an infection for which culture results of samples from the suspected site of infection remained negative. In contrast to infections occurring following 48 hours of admission to MICU, those occurring within 48 hours of admission were considered non-MICU acquired. Empirical antibiotic therapy was classified as "inappropriate" when an identified causative microorganism was found resistant after in-vitro sensitivity testing. Tuberculosis treatment usually involving a combination of ethambutol, isoniazid, pyrazinamide and rifampicin was considered as "one antibiotic". The diagnosis of community acquired pneumonia (CAP) was based on the guidelines of the American Thoracic Society.[9] Nosocomial pneumonia or hospital-acquired pneumonia (HAP) was defined as pneumonia that develops after 48 hours or more of hospital admission.[9] Ventilator-associated pneumonia (VAP) refers to nosocomial pneumonia that developed more than 48 hours following endotracheal intubation and mechanical ventilation.[10] Microbiological culture specimens obtained from patients admitted to MICU were classified according to their site as follows: blood, respiratory tract (for example sputum, endotracheal tube aspirates (ETT), bronchoalveolar lavage), stool, urine, cerebral spinal fluid (CSF), swab and other (for example ascitic and pleural fluid). Cultures were considered 'positive' when the growth of a potential pathogenic organism was observed and 'negative', when cultures yielded no growth or growth of commensal or colonizing microorganisms, or both, only: for example, blood cultures or cultures of tracheal aspirate with *Corynebacterium species* or tracheal aspirate cultures with *Candida species*, *Staphylococcus species* (coagulase negative) or *Haemophilus species*, other than *Haemophilus influenzae* were not considered pathogenic. Similarly, urine cultures yielding *Candida species* in the absence of any sign of infection were considered as colonization. Bronchoalveolar lavage was performed according to the technique described by Chastre et al,[11] and was examined microscopically for evidence of infection. Presence of bacteria and culturing was carried out semi-quantitatively on standard microbiological media. Descriptive statistical analysis was carried out using the Statistical Package for Social Sciences. Where appropriate, values are expressed as percentage, mean ± SD or range.

Results. During the study period, a total of 159 patients were admitted to the MICU. Eighty-seven patients (55%) were admitted for less than 48 hours, and were therefore not included in this DUR. One patient was still admitted 3 weeks after the end of the study period and was not included. From the 71 remaining patients, 54 (76%) fulfilled the entry criteria for this study. Their epidemiological characteristics are summarized in **Table 1**. From the 71 eligible patients, 54 (76%) were treated for presumed or proven infections, and received antibiotics **(Table 1)**. This corresponded with 280 (89%) of the 313 patient days. Most infections were non-MICU acquired. Respiratory infection accounted for 57% of all infections (MPI and non-MPI), with the majority being CAP (42%) followed by HAP (35%), and VAP (16%). A total of 159 antibiotics (134 intravenously [IV] and 25 orally) were administered to the 54 patients during their stay in MICU, corresponding with an average of almost 3 antibiotics per patient. Twelve patients (22%) received one antibiotic, 16 patients (30%) were managed with 2 antibiotics, 7 patients (13%) with 3 antibiotics, 11 patients (20%) with 4 antibiotics, and 8 (15%) with 5-8 antibiotics. Ceftriaxone was prescribed in 31 patients (57%) as the initial therapy: as the only antibiotic in 17 patients, and in combination with other antibiotics in 14 other patients (azithromycin IV in 10 patients, once with erythromycin IV once with ciprofloxacin IV once with clindamycin IV, and once in combination with metronidazole IV, and vancomycin IV). Antibiotics were given empirically in all but 6 (11%) patients: 5 patients receiving ceftriaxone IV as prophylaxis for gastro-intestinal bleeding and one patient was treated for *Helicobacter pylori*. Antibiotic usage was discontinued, due to non-justified initiation, in 11 (20%) patients after 24 hours, and 6 (11%) patients after 48 hours.

In these 54 patients, a total of 385 microbiology samples for culturing were taken throughout the study period, corresponding with more than one sample per patient per day. Twelve percent of the samples mainly originating from the respiratory tract (sputum, ETT, nasal, and oropharyngeal swabs) were considered "invalid" for analysis. Positive cultures were found in order of sequence: in respiratory tract samples (predominantly ETT)

Table 1 - Characteristics of study population (N = 54) admitted to the MICU for ≥ 48 hours and receiving antibiotic therapy for any suspected infection.

Characteristics	n	(%)
Male	17	(31.5)
Female	37	(68.5)
Age (mean + SD [range])	53 ± 19 [13-88]	
Nationality		
Qatari	34	(63)
Other Middle East countries	10	(19)
Indian subcontinent	7	(13)
Africa	2	(4)
Europe	1	(1)
Length of stay (mean + SD [range])	5.8 ± 6.9 [2-45 days]	
Total patient days	313	
2 days	12	(22)
3-4 days	26	(48)
5-7 days	7	(13)
> 7 days	9	(17)
Admission status		
Emergency department	34	(63)
Ward	20	(37)
Patients on antibiotics before admission to MICU	17	(31)
Mortality in MICU		
Total over study period	14/159	(8.8)
Study population only	6/54	(11.1)
Suspected source of infection		
Respiratory	31	(57)
Gastroenterology	9	(17)
Septicemia	6	(11)
Neurology	4	(7)
Nephrology	2	(4)
Other	2	(4)
Interventions and co-morbid conditions		
Mechanical ventilation	16	(30)
Central venous line	22	(41)
Renal impairment	10	(18.5)
Malignancy	10	(18.5)
Cor pulmonale	9	(17)
Liver impairment	7	(13)
Heart failure	6	(11)
COPD	5	(9)
Obesity	5	(9)
Cardiopulmonary arrest	3	(5.5)

MICU - medical intensive care unit, SD - standard deviation
COPD - chronic obstructive pulmonary disease

(13%), followed by blood cultures (12%), and urine and stool cultures (only 4% each). Cerebrospinal fluid, wound, and ear swab constituted the remainder of the samples (3%), and provided positive cultures in 10%. Upon admission to MICU, 186 samples were taken in our 54 patients for microbiological testing with clinical suspicion of infection, corresponding with approximately 3.4 samples per patient. From these, 50 cultures (27%) yielded positive results in 28 different patients. Sensitivity results were provided for all patients with bacterial infections (23/28 patients) but not routinely for patients with fungal infections (5/28 patients). Subsequently, the impact of the microbiological specimen analysis on establishing a microbiological etiology for these infections was assessed. Fifty-two percent of patients had an MPI: 18% with CAP, 18% VAP, and 11% with HAP **(Table 2)**. In the group of MPI, antibiotic sensitivity pattern resulted in change in EAB therapy in 12 of 23 patients (52%). In the group of patients with non-MPI, EAB was changed in 5 of the 26 patients (19%). No antibiotic course was discontinued due to negative culture results. Many patients were transferred to other units before the microbiological results became available.

A total of 30 patients (56%) received steroid therapy; methylprednisolone was used in 11 patients while hydrocortisone (100 mg IV every 8 hours) combined with fludrocortisone (50 mcg p.o. every 24 hours) was used in 9 patients as part of the sepsis protocol.[8] Details on the usage of steroids and the occurrence of yeast infection are provided in **Table 3**. Yeast infections developed in 43% (13/30) of patients. Six patients received methylprednisolone IV, 3 patients a combination of hydrocortisone IV, and fludrocortisone p.o. From the 24 patients not receiving steroids, 5 (20.8%) developed yeast infection. Yeast was mainly detected in sputum (9 specimens) and ETT secretions (8 specimens) while 2 patients developed candidemia.

Discussion. This DUR evaluates the current usage of anti-microbial agents in the MICU at our institution, and correlates it with: a) the infectious disease pattern, b) the causative microorganisms, and c) the patient's clinical outcome. Furthermore, the influence of the use of steroid therapy on the development of fungal infections was also evaluated. In our study, the patients' characteristics are comparable to that of other MICUs in other parts of the world,[3,12,13] with a mean age of 53 years with respiratory infections being the most common ones. The lower mortality rate (8.8% versus 23%) as well as the shorter LOS in the MICU (5.8 days compared to for example 8.2 days in the study of Schurink et al[3] might be due to the relative short study period. It also needs to be clarified that our MICU does not

Table 2 - Impact of microbiological cultures and sensitivity patterns on EAB therapy in patients with MPI respiratory infection (n = 13).

Respiratory infection	Patient identification/ Culture site	Empirical treatment	Cultured pathogen	LOS in MICU (days)	Switch to/reason	Sensitivity/patient outcome
CAP	#33/sputum	Ceftriaxone + azithromycin	*M. catarrhalis* + *H. influenzae*	2	No switch to cefuroxime/T	cefuroxime and TMP SMX /survived
CAP	#38/ETT	Ceftriaxone + azithromycin	*P. aeruginosa* + *K. pneumoniae*	2	No switch to cefuroxime/T	cefuroxime and ciprofloxacin/survived
CAP	#41/blood	Ceftriaxone + azithromycin 1 day	*S. pneumoniae*	3	Piperacillin tazobactam and ciprofloxacin/clinical deterioration and T	erythromycin and penicillin G/ survived
CAP	#31/ETT	Piperacillin-tazobactam	*E. cloacae* (1) + MRSA	4	No switch to meropenem and gentamicin/I No treatment for MRSA/T	meropenem and gentamicin/survived
CAP	#26/blood	Ceftriaxone + azithromycin	*K. pneumoniae*	4	No switch to cefuroxime/T	cefuroxime and amoxiclav/survived
HAP	#43/sputum	Piperacillin-tazobactam	*P. aeruginosa*	2	No switch/MDR	MDR
HAP	#28/blood and sputum	Meropenem + clindamycin	*Enterobacter cloacae* (1) + MRSA (sputum)	6	No switch to cefuroxime/I Vancomycin added	cefuroxime and TMP SMX/expired 6 days after admission at MICU
HAP	#25/sputum	Ceftriaxone + azithromycin	*P. aeruginosa* + MRSA	3	Piperacillin tazobactam/T No treatment for MRSA/T	intermediate sensitive to piperacillin-tazobactam and gentamicin/survived
VAP	#6/ETT	Ceftriaxone + azithromycin	*H. influenzae*	7	No switch to cefuroxime/I	cefuroxime/survived
VAP	#8/ETT	Ceftriaxone + azithromycin	*K. pneumoniae** (1) + MRSA (2) + *S. marcescens***(3)	42	(1) Piperacillin tazobactam followed by cefipime and followed by amoxiclav/A (2) + vancomycin/A (3) none/MDR	(1) amoxiclav (2) vancomycin (3) MDR /survived
VAP	#10/ETT	Ceftriaxone, 1 day	*K. pneumoniae*	3	No switch to cefuroxime/I	amoxiclav and cefuroxime/survived
VAP	#17/ETT	Ceftriaxone	*K. pneumoniae*	4	Piperacillin tazobactam/ I	amoxiclav, cephalotin and TMP-SMX/survived
VAP	#2/ETT	Cefepime + clindamycin, 3 days	*P. aeruginosa* + *S. marcescens*	10	Meropenem/A	meropenem/survived

CAP - community-acquired pneumonia, VAP - ventilated-acquired pneumonia, HAP - hospital-acquired pneumonia, EET - endotracheal tube, MRSA - methicillin-resistant *Staphylococcus aureus,* LOS - length of stay, MICU - medical intensive care units, MDR - multiple drug resistant organism, TMP-SMX - co-trimoxazole, T - patient transferred to ward before microbiological results became available, A - appropriate switch and/ or addition according to sensitivity patterns, I - inappropriate continuation of EAB therapy, * - cultures positive one month after admission to MICU, ** - cultures positive 1.5 months after admission to MICU, EAB - empirical antibiotic, MPI - microbiologically proven infection, *M. catarrhalis - Moraxella catarrhalis, H. influenzae - Haemophilus influenzae, P. aeruginosa - Pseudomonas aeruginosa, S. marcescens - Serratia marcescens, K. pneumoniae - Klebsiella pneumoniae, S. pneumoniae - Streptococcus pneumoniae, E. cloacae - Enterobacter cloacae.*

Table 3 - Details on the usage of steroid therapy.

Clinical condition	n of patients	Steroids used	n of patients (%)	n of patients with yeast (%)
Respiratory failure	9	Methylprednisolone IV	11(20)	6 (55)
CNS	1			
Neutropenia	1			
FUO	1	Hydrocortisone IV	4 (7.5)	2 (50)
Cancer	1			
Renal failure	2			
Severe sepsis and septic shock		Hydrocortisone IV + fludrocortisone oral	9 (17)	3 (33)
Steroid dependent asthma		Prednisolone oral	3 (5.5)	0
CNS	2	Dexamethasone IV	3 (5.5)	2 (67)
FUO	1			
Miscellaneous, no clinical indication for steroid usage		None	24 (44.5)	5 (21)
Total			**54 (100)**	**18 (33)**

CNS - central nervous system, FUO - fever of unknown origin, IV - intravenous

admit any surgical patients. Although the Acute Physiology and Chronic Health Evaluation II (APACHE II) was not used as a criterion of assessment, the co-morbid conditions of the patient reflect very well the seriousness of their illness.

Our study results show that 76% of all patients admitted for more for > 48 hours at MICU, and clinically suspected of having an infection were prescribed antibiotics corresponding with 89% of all patient days at this unit. A recent European study in an MICU setting revealed a more than 25% lower rate (62%) of antibiotic usage for presumed or proven infections in MICU, and this with a lower rate of microbiological sampling (0.64 versus 1.2 specimen per patient per day in our study), and a similar rate of positive microbiologically samples (30% versus 27% in our study).[3] Prevalence studies on the use of antibiotics in intensive care over the last decade revealed similar findings.[14,15] This implies that the threshold of suspicion of infection is much lower in our study population. Furthermore, consistent with the recent European study,[3] our observations revealed that despite the many microbiological cultures taken, and regardless of the isolated pathogen and its sensitivity pattern, these results barely had any impact on the antibiotic management at our MICU, and that empirical therapy was invariably continued. Whether this is due to a low potential for microbiological diagnostic procedures by itself, or inappropriate microbiological investigations requested by the MICU team needs to be determined and hence, needs further evaluation. Factors contributing to this phenomenon are the absence of any proven cultured pathogen, and like in our case the short stay at MICU for the majority of patients (52% were transferred within 3 days and 70% within 4 days). Although preliminary, these findings clearly highlight the need for a review of antibiotic prescribing policies as well as the monitoring of the antibiotic usage.

As in other studies, respiratory infections were the most frequently observed MPIs (68%), with gram-negative infections being the most common ones. After the treatment was initiated by on call staff at MICU, the discontinuation, within 24-48 hours in 31% of patients, was often suggested by the clinical pharmacist and endorsed by the MICU consultant. Ceftriaxone was mainly involved, as this antibiotic is very much the "standard" drug upon admission in this MICU: over half of patients received ceftriaxone. While this drug is the mainstay for treatment of meningitis, only 5 (9%) patients were admitted with a suspicion of a CNS infection, none of them were confirmed for bacterial meningitis.[16] Both HAP and VAP significantly contribute to morbidity, mortality, and escalating healthcare costs due to increases in antibiotic prescription and administration, and length of ICU stay. Colonization of the upper respiratory tract followed by aspiration seems to be the major pathogenetic mechanism for the development of nosocomial pneumonia, either in intubated or spontaneously breathing patients. The lack of solid data regarding the effect of microbiological cultures on the antibiotic therapy in an MICU setting is largely based on the inaccurte diagnoses, particularly of respiratory tract infections. The main problems of diagnosis in, particularly, lower respiratory tract infection are the differentiation of infection from colonization or contamination, and the isolation of a

reliable and true pathogen. Indeed, mechanical ventilation provides an excellent medium for all commensal and pathogenic microorganisms to thrive and colonize the respiratory tract. Pulmonary infiltrates on chest x-rays, and other clinical and laboratory criteria, such as fever, leucocytosis, purulent endotracheal secretions, and positive cultures, often leads to inaccuracy in diagnosing VAP. More invasive diagnostic sampling techniques (for example, protected specimen brush, protected catheter, protected mini-bronchoalveolar lavage bronchoscopic bronchoalveolar lavage), in addition to endotracheal aspirates and standard bronchoalveolar lavage, as diagnostic work-up of VAP suspected infections have proven to reduce the number of false positive cultures.[17-19] Consequently, the data from these studies revealed that fewer patients with VAP were exposed to EAB therapy without affecting clinical outcome. A more widely accessible strategy to limit the antibiotic use in MICU, is to initiate a broad-based empirical therapy, which is subsequently scaled-down upon availability of the microbiological cultures. However, in our experience this did not seem to be the on-going practice, probably due to shorter duration of stay of our patients in MICU (5.8 days), compared with patients in the study of Schurink et al[3] (8 days). However, the high rate of antibiotic usage on admission in patients with a low index of suspicion of infection can result in unwanted resistance, besides rendering further microbiological investigations obsolete.

The use of steroids in septic shock is extensively studied, and a treatment algorithm on their use is available.[8] In our study, patient numbers are too small to draw firm conclusions, but the concern of having higher risk of candida/yeast infections while on steroids is not justified as only 33% of septic patients receiving the advocated steroid regimen (200 mg IV hydrocortisone per 24 hours combined with an oral dose of 50 microgram fludrocortisone) developed candida, compared to 55% of patients receiving methylprednisolone for pulmonary and other conditions, and 21% receiving no steroids at all.

This study indicates that there is an urgent need for empiric and treatment antibiotic guidelines, to which strict adherence is essential and that similar DURs should be extended to other units in our hospital in order to assess anti-infectious management. Subsequently, the use of the prescribed antibiotic needs to be closely monitored, by for example, daily briefing and update between medical microbiology, infectious diseases, MICU (and medical staff after transfer from the MICU) and clinical pharmacy staff to assure justified usage of continuous antibiotics. For the time being, EAB treatment should be started without any delay, based on clinical suspicion, and guided by local MICU pathogen epidemiology, and antibiotic resistance patterns and on a de-escalating antibiotic strategy. Rotating EAB schedule, to limit the emergence of new multi-drug resistant pathogens combined with good communication between MICU team and microbiologists leading to rapid intervention in antibiotic strategy (cessation of unnecessary therapy or inappropriate antibiotic prescribing) are imperative strategies.[20] Furthermore, the adoption of this policy should be accompanied by other infection control practices aimed at reducing antimicrobial resistance and nosocomial infections. Finally, similar DURs should be extended to other units in our hospital in order to assess anti-infectious management.

Acknowledgment. The authors would like to thank Dr. Noora Obaidan, Director of Pharmacy, and Dr. Abdul Latif Al-Khan, Chairman of Department of Medicine and Head of Infectious Diseases, for their encouragement in performing this study.

References

1. Kollef MH. Optimizing antibiotic therapy in the intensive care unit setting. ***Crit Care*** 2001; 5: 189-195.
2. Scott G. Prevention and control of infections in intensive care. ***Intensive Care Med*** 2000; 26 Suppl 1: S22-S25.
3. Schurink CA, Hoitsma M, Rozenberg-Arska M, Joore JC, Hoepelman IM, Bonten MJ. Do cultures contribute to optimization of antibiotic therapy in the intensive care unit? ***Int J Antimicrob Agents*** 2004; 23: 325-331.
4. Hamad Medical Corporation - Annual Report 2003. Available from URL: http://hmc.org.qa
5. Lefering R, Neugebauer EA. Steroid controversy in sepsis and septic shock: a meta-analysis. ***Crit Care Med*** 1995; 23: 1294-1303.
6. Bernard G, International Sepsis Forum. The International Sepsis Forum's controversies in sepsis: corticosteroids should not be routinely used to treat septic shock. ***Crit Care*** 2002; 6: 384-386.
7. le Roux P. New concepts in treatment of sepsis. ***SADJ*** 2004; 59: 208-209.
8. Prigent H, Maxime V, Annane D. Clinical review: corticotherapy in sepsis. ***Crit Care*** 2004; 8: 122-129.
9. American Thoracic Society. Guidelines for the management of adults with community-acquired pneumonia. ***Am J Resp Crit Care Med*** 2001; 163: 1730-1754.
10. Cook D. Ventilator associated pneumonia: perspectives on the burden of illness. ***Intensive Care Med*** 2000; 26: S31-S37.
11. Chastre J, Fagon JY, Domart Y, Gibert C. Diagnosis of nosocomial pneumonia in intensive care unit patients. ***Eur J Clin Microbiol Infect Dis*** 1989; 8: 35-39.
12. Hug B, Rossi M. A year's review of bacterial pneumonia at the central hospital of Lucerne, Switzerland. ***Swiss Med Wkly*** 2001; 131: 687-692.
13. Esen S, Leblebicioglu H. Prevalence of nosocomial infections at intensive care units in Turkey: a multicentre 1-day point prevalence study. ***Scand J Infect Dis*** 2004; 36: 144-148.
14. Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoin MH, et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee. ***JAMA*** 1995; 274: 639-644.

15. Bergmans DC, Bonten MJ, Gaillard CA, van Tiel FH, van der Geest S, de Leeuw PW, et al. Indications for antibiotic use in ICU patients: a one-year prospective surveillance. ***J Antimicrob Chemother*** 1997; 39: 527-535.
16. Deleu D. Neurology in clinical practice: an algorithmic approach [online]. Available from URL: http://www.neuroweb.us
17. Kollef MH, Ward S. The influence of mini-BAL cultures on patient outcomes: implications for the antibiotic management of ventilator-associated pneumonia. ***Chest*** 1998; 113: 412-420.
18. Bonten MJ, Bergmans DC, Stobberingh EE, van der Geest S, De Leeuw PW, van Tiel FH, et al. Implementation of bronchoscopic techniques in the diagnosis of ventilator-associated pneumonia to reduce antibiotic use. ***Am J Respir Crit Care Med*** 1997; 156: 1820-1824.
19. Fagon JY, Chastre J, Wolff M, Gervais C, Parer-Aubas S, Stephan F, et al. Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. A randomized trial. ***Ann Intern Med*** 2000; 132: 621-630.
20. Hughes MG, Evans HL, Chong TW, Smith RL, Raymond DP, Pelletier SJ, et al. Effect of an intensive care unit rotating empiric antibiotic schedule on the development of hospital-acquired infections on the non-intensive care unit ward. ***Crit Care Med*** 2004; 32: 53-60.