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Physicians compliance with antimicrobials' de-escalation in intensive care units in jordan

Jamal Wadi MD, FIDSA[1]*, Sahar Al Shair PharmD[2], Waseem Abu Ashour PharmD[2], Mohammad Rabi PharmD[3], Haifa Petro RN[4], Amani Romman RN[4], Yaseen Alastal M.D[5], Rula Rashed M.D[5], Gheida Melhem PharmD[6]

1 Office 11.Third Floor.The Medical Center, Jordan Hospital Medical Center Adeeb Wahba Street, Amman – Jordan 11184,
2 Department of Pharmacy, 30 Adeeb Wahba Street, Jordan Hospital, Amman – Jordan 11184
3 Department of Pharmacy, Al Khalidi Medical Center, 39 Ibn Khaldoon Street, Amman – Jordan 11183
4 Infection Prevention and Control Division, Al Khalidi Medical Center, 39 Iben Khaldoon Street, Amman – Jordan 11183
5 Internal Medicine Department , Specialty (Al Takhassusi) Hospital, Jaber Ibn Hayyan Street. Amman – Jordan
6 Pharmacy Department, Specialty (Al Takhassusi) Hospital, Jaber Ibn Hayyan Street. Amman – Jorda

Correspondence:

jamalwadimd@yahoo.com

Abstract

Background: To evaluate physicians' behavior toward antimicrobials de-escalation for their patients should an opportunity come into view.

Methods: A prospective observational study held in three hospitals. Data were obtained prospectively for ICU patients with the diagnosis of sepsis i.e. systemic sepsis of any source, multi-organ dysfunction syndrome, and septic shock and were started on broad-spectrum antimicrobial agents (BSA). Failure to de-escalate was considered if a known culture was available and was susceptible to a narrower antimicrobial agent; hitherto the treating physician did not de-escalate. Excluded from the study patients who were not started on BSA, were on antimicrobial prophylaxis or there was no clear indication for starting BSA, also patients whom their microbiological diagnoses were not available or the pathogen was only susceptible to the initially started BSA.

Results: One hundred and nineteen patients were followed; their charts were reviewed. There was 69 (58%) male and 50 (42%) female with mean ages of 59.3 and 68.6 years respectively. Eight (6.7%) patients were de-escalated to narrower spectrum antimicrobials. None of: APACHE II score, comorbidities, patients'outcome while on BSA, sepsis-predisposing clinical diagnosis and microbiological diagnosis significantly encourage physicians for de-escalation. The commonest initial antimicrobials used were Meropenem, Pipracillin/Tazobactam and Imipenem.

Conclusion: The majority of physicians did not de-escalate when it ought to be done. The concept of de-escalation has to be stressed upon widely among treating physicians.

Keywords: De-escalation, Broad-spectrum antimicrobials, physicians' behavior, prudent antimicrobials' use, bacterial resistance.

Introduction

Prudent use of antimicrobials is a worldwide necessitydue tor-apid acquisition of resistance among bacteria disabling their potential use. The wide spread of multidrug resistant bacteria urges physicians to assume prudent antimicrobial use, avoiding the use of broad spectrum antimicrobials (BSA) should the microorganism and its antimicrobial susceptibility pattern are known and can be targeted with a narrower one i.e.de-escalation. (1)

Currently there are useful BSAs available for use in the empiric treatment of seriously sick patients. They comprise agents of different classes; carbapenems, β-lactam β-lactamase inhibitors, glycylcyclines, respiratory quinolones and cephalosporins including the new fifth generation ceftaroline fosamil. Combination antimicrobials therapies also provide broad-spectrum coverage.

Due to their activity, it is always prudent to start with BSA when treating seriously septic patients who are admitted to ICUs. However, the practice of continuing patients on BSA therapy should always come under scrutiny for they may contribute to collateral damage and increasing resistance in patients and community at large. (1, 2) For this reason, the idea of de-escalation was in place as soon as BSA was widely used. The idea behind de-escalation is to utilize those agents when initially, empirically are needed, optimizing appropriate therapy in patients, however, should a microbiological diagnosis was made; one would de-escalate to cover that specific pathogen. Unfortunately many physicians reject this proper behavior, and are not willing to de-escalate in spite of a specific pathogen and its susceptibility is known. (3, 4)

After many years of introducing the idea of de-escalation, the aim of this study is to evaluate physicians' attitude in this part of the world; whether they de-escalate from BSA agents to a more specific suitable agent or not when a known microbiological diagnosis was available for them. We plan to test this hypothesis of whether physicians adopt the attitude of de-escalation or it is just an illusion. (5)

Materials and Methods

Setting

A multicenter prospective study held in Amman –Jordan from March to August 2012. It included three hospitals; two teaching and one community service hospitals with total of 52 ICU beds, the three hospitals do not have antimicrobial restriction policies. The internal review boards approved the study in the teaching hospitals and the medical administrator approved it in the community hospital. Data were collected prospectively from patients'files who fulfill inclusion criteria; Study teams collected data without having any influence on patient' management; data collection was made by medical residents and PharmD's not directly involved in ICU patients care or doing recommendation about antimicrobial therapy, patients were managed by their attending physicians; internists, intensivests and surgeons.

Inclusions and exclusion criteria

Patients were included if they reside in ICU, carry one of the major sepsis syndromes such as severe community-acquired pneumonia (CAP), ventilator-associated pneumonia (VAP), catheter-associated urinary tract infections (CAUTI), severe urinary tract infections (UTI), central line-associated blood stream infection (CLABSI), sepsis/bacteremia of undefined source and blood cultures were available, skin and skin structure infection (SSTI) intra-abdominal infection (IAI) and meningitis, i.e infections resulting in significant systemic sepsis, multiorgan dysfunction syndrome (MODS) and septic shock,and were started on BSA agents as mono-therapy or in combination. We consider failure to de-escalate, if a culture was available and it was susceptible to a narrower antimicrobial agent and the treating physician did not de-escalate. Excluded from the study all patients who were not started on BSA agents, were on antimicrobial prophylaxis or there was no clear indication for the use of BSA agents, also patients whom their microbiological diagnoses were not available (known to the treating physician) or the pathogen was only susceptible to the initially started BSA agent(s). The following available agents were considered as BSA agents: carbapenems, β-lactam β-lactamase inhibitors, glycylcyclines, respiratory quinolones and the parenteral third and fourth generations cephalosporins. Combination antimicrobials therapies prescribed in treating seriously sick patients and intended to provide BSA coverage with or without vancomycin or teicoplanin were included.

Outcome measures

The primary outcome measure is to evaluate the proportion of physicians who de-escalated from BSA agents to an appropriate pathogen-specific antimicrobial when the pathogen is identified in accordance with previously published recommendations. (6) Secondary outcome measures were if physicians' behavior or attitude were influenced by patients' initial improvement, comorbidities, clinical diagnosis, microbiological diagnosis, outcome and APACHE II score.

Table. Features, characteristics and results of 119 patients included in de-escalation study for patients treated in two teaching and one community hospitals ICU's in Amman – Jordan for the period of March August, 2012.

	De-escalated N (%)	Not De-escalated N (%)	P value
Age mean, both genders (Years)	60	63.5	0.67@
Primary outcome measure for patients in whom physicians de-escalated from BSAs	8 (6.7)	111 (93.3)	--
Hospitals Teaching Community	79 (66) 40 (34)	--	--
APACHE II <9 10 -15 16 – 20 >20	 2 2 3 1	 22 33 24 32	0.64*
Clinical Diagnosis VAP UTI Septicemia SSTI Undefined	 0 3 5 0 0 0	 8 10 56 3 29 5	0.11*
Comorbidities (DM, Lung Disease, Solid Malignancy, Hemato Malignancy, Immunosuppressive, Heart failure)	7/8 (87.5%)	85/105 81%)	0.65*
Microbiological diagnosis N *E. coli* *Candida spp.* *Staphylococcus aureus* *Enterococcus spp.* *Klebsiella pneumonia* *CoNS* *Serratia marsecence* *Acinetobacter spp.* Others	6 4 0 0 1 0 0 0 0 1	57 12 7 5 2 10 3 2 7 8	0.34*
Commonly used antimicrobials Meropenem PIP/TAZ Imipenem Teicoplanin Vancomycin Quinolones	 2 5 1 0 0 0	 31 37 29 2 1 1	0.79*
BSAs duration N mean (Days)	8 6.75	107 7.72	0.67@
Outcome N Improved and discharged from ICU Partially improved Did not improve Death	8 5 1 0 2	107 55 16 3 33	0.92*

N: number of patients available in each category and percentage (%) where appropriate
*Pearson chi square test
@ t-test for equality of means
APACHE II: Acute Physiologic and Chronic Health Evaluation score number two
BSA duration: Number of days broad spectrum antimicrobials were used on patients

Statistical analysis

Data were uploaded to SPSS. Proportion of physicians who de-escalated was calculated compared with those who did not. In addition, to analyze secondary variables what affected physicians' attitude towards de-escalation, student t-test and χ^2 were used to demonstrate if there were differences among different parameters within the subgroups. $P \leq 0.05$ is considered significant.

Results

One hundred and nineteen patients' charts were prospectively reviewed. Seventy-nine (66%) of patients were recruited from teaching hospitals and 40 (34%) from the community hospital.There was 69 (58%) male and 50 (42%) female patients with mean ages of 59.3 and 68.6 years respectively. Eight (6.7%) patients were de-escalated to narrower spectrum antimicrobials upon having a microbiological diagnosis. Patients' APACHEII score was similar for both; de-escalation or not sides and no significant difference was found ($p = 0.64$). The most frequent diagnosis was septicemia of undefined source (60), this was followed by severe CAP (38), UTI (13), and VA (8) patients, no significant statistical difference was found between groups on either side ($p = 0.11$). Comorbidities included: diabetes mellitus, lung disease, solid malignancy, hematological malignancy, Immunosuppressive treatment and heart failure, no significant statistical difference among groups on either side ($p = 0.65$).The microbiological diagnosis was not significantly different between the two sides ($p = 0.34$), seven patients among those who were not de-escalated had candida in addition to bacterial sepsis. The commonest initial antimicrobials used were Meropenem followed by Pipracillin/Tazobactam and Imipenem. Carbapenem combined were used 42% of times and pipracillin/tazobactam in 20.5%. Quinolones, were used in 24 Patients in either arm, vancomycin in 22 and teicoplanin in 27 patients-use, however the last three antimicrobials were used in combination with a carbapenem, or pipracillin/tazobactam. Tigecycline was used in one patient.

There was no significant statistical difference in BSA duration between those who were de-escalated versus those who were not, 6.75 days versus 7.72 days ($p = 0.67$). Patients outcome; improvement and discharged from ICU, partially improved, did not improve and those who died did not show significant statistical difference between the two groups ($p = 0.92$).

Discussion

The concept of de-escalation started about two decade ago after BSA agents largely emanated into practice and found useful in combating sever sepsis syndromes. A major concept was introduced; to use an appropriate agent "to get it right the first time" so that we improve therapeutic outcome while cutting down on resistance. (7)Nonetheless, BSA agents were found not devoid of flaws should an unjustified regimen, duration and frequency of therapeutic dosing implemented, where CDI, MRSA, VRE, ESBL and the relatively late KPC are major culprit of wide and indiscriminate use of BSA agents. (8, 9, 10, 11, 12)

The aim of this study is to evaluate physicians behavior toward de-escalation, we found that only 8 (6.7%) out of 119 physicians de-escalated to narrow-spectrum antimicrobials when in fact the opportunity was available for them i.e. they had microbiological diagnoses and susceptibility pattern compatible for de-escalation. Moreover, we assessed physicians attitude towards de-escalation whether it was modified based on patients' co-morbidities, APACHE II score, underlying clinical disease and microbiological findings whether gram-positive or gram-negative; none of the previous variables affected physicians' behavior ($p > 0.05$). Patients who were on short or long term regimens made no difference for physicians' decision regarding de-escalation ($p > 0.05$).

In conclusion, the vast majority of physicians are not de-escalating when it ought to be done. The concept of de-escalation has to be informed widely among treating physicians backed up by the hospital clinical microbiologist. A caveat in the study includes small number, which precludes a firm conclusion about the intent to de-escalate-or-not based on variables like co-morbidities, APACHE II score, underlying clinical disease and microbiological findings whether gram-positive or gram-negative.

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References

1. Kollef, MH. Broad-Spectrum antimicrobials and the treatment of serious bacterial infections: Getting it right up front. Clinical Infectious Diseases 2008; 47: S–-13.
2. Paterson, DL. Collateral damage" from cephalosporin or quinolone antibiotic therapy. Clinical Infectious Diseases 2004; 38 (Suppl. 4): S34–-5.
3. Davey, PG. and Marwick, C. Appropriate vs. inappropriate antimicrobial therapy. Clin Microbiol Infect. 2008; 14 (Suppl. 3): 1–-21.
4. Phee, L. et al. De-escalation of antimicrobial therapy inmgram-negative sepsis Easier said than done? Critical Care 201 ; 15 (Suppl. 1):P219.
5. Jan, J., Waele, D. De-escalation after empirical meropenem treatment in the intensive care unit: Fiction or reality? Journal of Critical Care 2010;:25 (;): 641-646.
6. Hooton, T. et al. Infectious diseases society of america and the society for healthcare epidemiology of america guidelines for developing an institutional program to enhance antimicrobial stewardship. Clinical Infectious Diseases 2007; 44: 15–-77.
7. Kollef, MH. Appropriate empirical antibacterial therapy for nosocomial infections getting it right the first time. Drugs 2003; 63 (20): 2157-2168.
8. Moi¨ra, J.,eTalpaert, L., Guduru,oG., Symons, B. Wade, P. Impact of guidelines and enhanced antibiotic stewardship on reducing broad-spectrum antibiotic usage and its effect on incidence of Clostridium difficile infection. J Antimicrob Chemother 2011; 66: 216–-2174.
9. Wilcox, MH. The tide of antimicrobial resistance and selection. International Journal of Antimicrobial Agents 200.; 3 : S3-S6-S10.
10. aBratu, S., Brooks, S., Burney, S.,pKochar, S., Gupta, J., Landman, D., Quale, J. Detection and spread of escherichia coli possessing the plasmid-borne carbapenemase KPC-2 in Brooklyn, New York. Clinical Infectious Diseases 2007; 44: 97–-5.
11. Urban, C., Bradford, P., Tuckman, M., Segal-Maurer, S., Wehbeh, L.e Grenner, R., Colon-Urban, N.l James, J. Carbapenem-Resistant escherichia coli harboring klebsiella pneumonia carbapenemase b-lactamases associated with long-term care facilities. Clinical Infectious Diseases 2008; 46:e12–-30.
12. Kenneth, M., Wener,dr., Howard, S., Gold, S.. Wright, B., Yehuda, i. treatment with fluoroquinolones or with β-Lactam β-Lactamase inhibitor combinations is a risk factor for isolation of extended-spectrum β-Lactamase-Producing klebsiella species in hospitalized patients. Antimicrobial Agents and Chemotherapy 201y; 54 (5): 201–-2016.