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Vancomycin Utilization Evaluation in a teaching hospital: A case- series study in Iran.

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ABSTRACT

Background: Increasing antimicrobial resistance is now a critical point of human being in the world. Especially wide spectrum antibiotics resistance germs like vancomycin-resistant enterococci (VRE) should be dealt as soon as possible as an emergency conflict. Our study tries to reveal the amount of irrational use of vancomycin in a teaching hospital in Iran.

Methods: We elected the whole inpatients that received vancomycin between February 2007 and May 2008.

Results: Forty four out of those 45 patients had inappropriate indication and dosing regimen of vancomycin (97.7%). The most use of vancomycin was recorded in hematology – oncology ward and then Intensive Care Unit (ICU). Culture responses were negative despite great clinical evidence of infection.

Conclusion: Vancomycin irrational use was high compared to other countries and it could be concerned as a major health problem by health policy makers and physicians to deal. However more detailed researches are needed to reveal the other aspects of this problem. Implementation of antibiotic protocols and standard treatment guidelines are recommended.

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Introduction

Today, antibiotic misuse and over prescription has become a major health problem in societies because of increasing number of multi drug resistant specimens and crisis of no new and effective antibiotics availability. Despite the large amount of antibiotic prescription guidelines and warnings to doctors, there is high numbers of inappropriate antibiotic use in outpatient and inpatient settings (1).

Almost align with antibiotics discoveries, antibacterial resistance develops. Resistant bacterial strains found in hospitals at first but spread in communities' quickly, out patients' settings and through all over the world (1). Over prescription of antimicrobial drugs, antibiotic sales as over the counter drugs and people self medications without referring to doctors lead to critical increasing in antibacterial resistance and (2).The rapid emergence of multi drug resistant organisms such as Methicillin-Resistant Staphylococcus Aureus (MRSA) and Vancomycin-Resistant Enterococci (VRE) is considered a big issue in medical practice (2). Treatment of these

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organisms cost much in health care expenditures, either the drug prices or the long inpatient care expenses.

One of the early and important steps to establish guidelines of drug use in hospitals is detecting the wards and departments that in which drugs are highly used. The health policy makers need precise data of vancomycin usage and indications in hospitals to set useful strategies for rational use of it. However the relationship between hospital antibiotic use and antimicrobial resistance is unclear yet.

Recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC) (3) were applied to evaluate vancomycin usage pattern in a Teaching Hospital in Tehran.

Patients and Methods

The study was conducted in a teaching hospital in Iran between February 2007 and May 2008. The hospital has 15 specialty and 5 subspecialty wards.

A comprehensive questionnaire was designed. Demographic characteristics of patient, the cause of admission, the date of hospitalization and antibiotic prescription, the medical history, indication of vancomycin administration, dosing regimen, duration of infusion, duration of treatment, history of allergy to food and drugs, fever detection, laboratory data, blood culture and antibiogram requests were recorded.

During the study period, the entire inpatients that were receiving vancomycin in their therapeutic profile were evaluated. The previously designed form was completed for each of them. Totally forty five patients were assessed in the study period.

In addition, appropriateness of prescribed doses and intervals, route of administration, necessary laboratory and clinical monitoring parameters, drug interactions, laboratory data results including microbiological culture/ sensitivity testing during the treatment period were determined.

Descriptive analyses of data were performed using SPSS software (version, 11).

Results

A total of forty five patients entered to the study. Twenty seven (60 %) of patients were male and eighteen (40%) were female. The mean age of them was 40.7 years old.

Most of the patients received vancomycin were in hematology – oncology ward (71.1%) and ICU (Intensive Care Unit) (8.16%), respectively.

Leukemias including Acute Myelogenous Leukemia (AML) and Acute Lymphoblastic Leukemia (ALL) were the most common reasons of admission. The other reasons of admission of patients in details are shown in table 1.

The most common indication for vancomycin prescription was fever due to Neutropenia and fever with unknown origin (FUO). Hematologists and otolaryngologists were the most prescribing physicians. Only one case out of forty five (2.2%) was received vancomycin consistent with mentioned indication in guidelines.

Thirty three (73.3%) patients had at least one serum creatinine level on their profiles. Thirty nine (86.6%) patients received vancomycin 1 gr every 12 hours and six of them (13.3%) received 500 mg every 8 hours.

Five patients (11.11%) had at least one result of serum creatinine level more than 1.5mg/dl

during treatment period and dosage adjustment was not done for four (80%) of these patients. Four patients received inappropriate dose of vancomycin based on serum creatinine level and 6 patients received incorrect dose as 500mg every 8 hours according to their disease. Totally 10 patients (22.2%) received inappropriate dose of vancomycin.

Thirteen (28.8%) patients had no culture requests in their profiles while they received vancomycin for treatment purposes. No culture results were found for 18 (40%) patients despite the fact that it was ordered by physician in charge. Four (8.8%) patients had negative culture results while ten (22.2%) had positive culture responses.

Only in one case (2.2%) vancomycin was prescribed according to antibiogram results.

Two cases (4.4%) experienced red neck man syndrome during administration. Twenty out of forty five patients (44.4%) received another nephrotoxic drug accompanying with vancomycin. The frequency of patients in different variables studied is shown in Table 1.

Discussion

Today the methicillin resistant staphylococcus has become a major health care problem and its resistance to vancomycin is increasing. For example the percentage of methicillin resistant staphylococcus aureus (MRSA) has increased from 35.9% to 64.4% during 1992 till 2003 in the United State hospitals (4). The significant and incorrect use of wide spectrum antibiotics led to this problem.Our study revealed that the major administration of vancomycin is in hematology- oncology ward, but in an observational study in Siriraj hospital in Thailand, there was significant use of vancomycin in pediatrics, surgery and ophthalmology wards (5) and in a Brazilian teaching hospital, 81.7% use of vancomycin was in intensive care unit (6).

The major indication of vancomycin administration was neutropenic fever (37.7%). They received vancomycin as soon as neutropenic fever was begun while use of vancomycin is discouraged for Empiric antimicrobial therapy for a febrile neutropenic patient, unless initial evidence indicates that the patient has an infection caused by gram-positive microorganisms and the prevalence of infections caused by MRSA in the hospital is substantial

Table 1. Variables accounted in vancomycin received patients.

Variables		Number of patients (%)
Hospitalization ward:		
	Hematology	32 (71.11)
	ICU(Intensive Care Unit)	4 (8.16)
	Vascular surgery	3 (6.12)
	ENT (Ear, Nose and Throat)	3 (6.12)
	General surgery	3 (6.12)
	Total	45 (100)
Reason for admission:		
	Acute Myelogenous Leukemia (AML)	16 (35.55)
	Acute Lymphoblastic Leukemia (ALL)	8 (17.77)
	Fractures	3 (6.66)
	Aplastic Anemia (AA)	2 (4.44)
	Multiple Myeloma (MM)	2 (4.44)
	Aorta Aneurism	2 (4.44)
	Lymphoma	2 (4.44)
	Pancytopenia	2 (4.44)
	Chronic Lymphoblastic Leukemia (CLL)	1 (2.22)
	Cellulitis	1 (2.22)
	Multiple trauma	1 (2.22)
	Fever of unknown Origin (FUO)	1 (2.22)
	Laparatomy	1 (2.22)
	Cardia cancer	1 (2.22)
	Frontal sinus mucocele	1 (2.22)
	Sinusitis	1 (2.22)
Physicians' specialty:		
	Hematologist- oncologist	33 (73.33)
	Otolaryngologist	4 (8.88)
	Vascular surgeon	2 (4.44)
	Vascular surgeon	2 (4.44)
	General surgeon	2 (4.44)
	Cardiologist	2 (4.44)
	Orthopedic surgeon	2 (4.44)
Indications of vancomycin administration:		
	Neutropenic fever	17 (37.7)
	Fever of Unknown Origin (FUO)	12 (26.64)
	Cellulitis	4 (8.88)
	Sinusitis	2 (4.44)
	Prophylaxis of post-orthopedic surgery infection	2 (4.44)
	Pneumonia	1 (2.22)
	Abdominal abscess	1 (2.22)
	Oral cavity infection	1 (2.22)

according to CDC criteria(7). Although in our study, vancomycin prescribed for neutropenic patients at the early stage of symptom beginning and continued even after the fever stopped, however the IDSA (Infectious Diseases Society of America) 2010 guideline for the use of Antimicrobial Agents in Neutropenic Patients with Cancer discourages vancomycin usage for adults without any complications (e.g., hypotension, pneumonia, MRSA infection) and recommends choosing an anti-pseudomonas β-lactam agent, such as cefepime, a carbapenem (meropenem or imipenem-cilastatin), or piperacillin-tazobactam as monotherapy in high risk patients that require hospitalization. It confirms that if patient met the criteria for use of vancomycin, we can use it and when patient becomes afebrile in 3-5 days, we should narrow the spectrum according to antibiogram results (8).

Here, reported 97.7 % inappropriate use of vancomycin while in another study conducted by Junior and coworkers, this amount was 65.7% during the first 24 hours and 67% at 72 hours according to CDC criteria (6).

Some of our patients had high clinical evidences of infection despite the negative culture results; which may be due to incorrect and inaccurate techniques of providing blood cultures or laboratory processes. Administration of a single stat dose of antibiotics in emergency room may also account for negative culture results. So, unless these factors omitted or ruled out from practice, it is not logical to consider all vancomycin prescribed patterns as irrational.

The rate of red man syndrome in our patients received vancomycin was 2.2 % and it was in the afternoon shift and due to short time infusion. Our rate is higher than 1.6% prevalence in children received vancomycin in Toronto, Canada pediatric study (9). In our institution, in morning work shift, nurses were more experienced in vancomycin administration. However new studies support longer infusion to one hour and increasing the volumes of dilution to minimize the sides effects and improve the patients' outcomes (10).

About 44% of our patients received another nephrotoxic drug simultaneously with vancomycin without frequent renal function monitoring. Nephrotoxicity is common with vancomycin especially amongst elderly patients because of lower kidney function. In one study in USA, the risk factors of vancomycin associated nephrotoxicity were compared between young and elderly hospitalized patients. Nephrotoxicity was significantly higher in elderly patients (11). It seems that physicians and nurses should be more cautious about vancomycin potential harms especially in elderly patient and high risk patients with multiple risk factors.

In conclusion, the following hints are recommended to achieve rational use of vancomycin and avoiding the enhancement of VRE (Vancomycin Resistant Enterococci):

1. Implementation the vancomycin use guideline modified according to local resistance pattern in hospitals
2. Conducting antibiotic usage review studies
3. Sending periodically feedbacks to physicians and nurses involved mostly in vancomycin administration
4. Setting pharmaceutical and therapeutic infection control committees in hospitals to discuss issues regarding antibiotic usage patterns and approaches
5. Reevaluating laboratory tests and processes related to infection control.

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