

Original Article

Drug Utilization Evaluation of Vancomycin in Pediatric Department

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Abstract

Background: Increasing reports of Vancomycin resistance have raised concerns about effectiveness of this drug. One of the most important factors of resistance emergence is no adherence of physician to principles of antibiotic therapy. This study is a drug utilization evaluation (DUE) of Vancomycin in pediatric ward to assess appropriateness of drug regimens and to find possible problems in clinical practices that may necessitate reconciliation to improve Vancomycin use.

Materials and Methods: This prospective study was done for 1 year from October 2014 to September 2015 at Khalij Fars General Hospital in Bandar Abbas. Data including patients' demographics, paraclinic, diagnosis, vancomycin dose, and treatment duration were collected. The concordance of practice with standard guidelines (CDC, ASHP, and IDSA) and principles of antibiotic therapy was assessed. Results were analyzed by SPSS 20.

Results: 102 medical records were reviewed in this study. Pneumonia (60=59%) and sepsis (22=21.5%) were the most common diagnosis. Sampling was done in 6% of patients with 2% antibiogram. Vancomycin was administered appropriately in 56.9% percent of patients with no sex difference (PV= 0.55) but age with significant difference (PV= 0.017). Over use was in a great proportion of patients (36cases=35%) as unnecessary, improper combination and broad spectrum regimen.

Conclusion: Vancomycin was overused irrationally in a great proportion of patients. There was no serum level monitoring. Microbial resistance, serum trough level monitoring programs and continuous medical education for physicians can be effective in rational use of antibiotic.

Keywords: Vancomycin, Evaluation, Rational Use, Pediatrics

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Introduction

The majority of admitted inpatients are given antimicrobials as therapy or prophylaxis during their

hospital stay. It has been shown that at least fifty percent of antimicrobial prescriptions are unnecessary. These irrational uses are due to inappropriate prophylactic antimicrobial prescribing, staying on

empiric therapy in a stable patient without positive cultures, and no information about susceptibility patterns of common pathogens. Antimicrobial over prescription increases the costs of health care, arise super infection due to antimicrobial-resistant bacteria, as opportunistic fungi, and may raise the likelihood of an unwanted drug side-effects. On the other hand, no consumption in an urgent condition at the bedside may also result to critical results. Antibiotics should be used as guidelines only and sometimes changed pursuant to medical judgment relative to individual patient needs¹. Vancomycin has a narrow and specific antibacterial spectrum against Methicillin resistant *Staphylococcus aureus* (MRSA), penicillin resistant *S.pneumonia* and resistant enterococcus infections and is saved for this serious and constantly growing public health concerns²⁻⁴. Also secondary resistance to vancomycin use is an important challenge⁵. Drug utilization evaluation has been found as an effective method to further interventions that will approve treatment outcomes and cost-effectiveness of the drug therapy⁶ and it is more important to control rational use of antibiotic to prevent resistance by continuing medical education (CME) course⁷. To achieve this target, true antibiotic selection consistent with guideline criteria and right through concentration are required⁸. We conducted this drug utilization evaluation (DUE) study in pediatric ward to determine rate of rational use of Vancomycin according to the standard guidelines. The rate of positive culture and antibiogram are low and therapeutic regimens are usually syndrome based and notifying patient's host factors. It is necessary to understand defects in Vancomycin use to find a solution and save this highly valued antibiotic for common perilous infections by resistant *Staphylococcus* and *Pneumococcus* with other less effective and expensive treatments.

Methods

This prospective study was carried out to evaluate the utilization of vancomycin from October 2014 to September 2015 in one year as census on all pediatric patients who received vancomycin. The study was conducted in Khalij Fars Hospital, a general hospital with 255 beds including 25 pediatric and 10 NICU ones in Bandar Abbas. Vancomycin administration

was assessed according to CDC, ASHP and IDSA guidelines. Predesigned data collection form was implemented in this study including sex, age, weight, creatinine, CBC, platelet, diagnosis, microbiological culture/sensitivity testing and occurrence of adverse drug reaction as hearing loss, tinnitus, renal failure, thrombocytopenia, co-administered antibiotics, vancomycin dose, result of treatment, infectious disease specialist consultation. Vancomycin utilization was evaluated by a pediatric specialist, a neonatologist and a pediatric infectious disease subspecialist. Glomerular Filtration Rate (GFR) was calculated for all patients using Cockcroft-Gault formula as an estimation of creatinine clearance. Results were reported as appropriate and inappropriate use due to dose per kg of body weight based on renal function tests, initial platelets count, diagnosis, culture and antibiogram, concurrent diseases and drugs as A: Appropriate, B: Inappropriate, (B1: Unnecessary, B2: Age, B3: Concomitant Disease, B4: Insufficient Spectrum, B5-1: Low Broad Spectrum, B5-2: High Broad Spectrum, B5-3: Unnecessary Combination of Two Similar Spectrum Antibiotic, B5-4: Ineffective, B6-1: Low Dose, B6-2: High Dose, B7: Improper Combination, B8-1: Short Duration, B8-2: Long Duration. Dose difference more than 20% was considered as incorrect dose. The serum concentrations of vancomycin were not measured. (Not available). Information was collected and data were analyzed using SPSS 20 software.

Results

During 12 months of study period, 102 patients (46 males and 56 females without significant difference, P value= 0.55) received Vancomycin. The age of patients are showed in Table 1. Diagnosis was made mostly by clinic and imaging and lesser with other paraclinical techniques as Table 2. Number and percent of appropriate (58cases=56.9%) and inappropriate (44cases=43.1%) use of Vancomycin based on studied factors are shown in Table 3. Appropriateness of vancomycin use based on culture with antibiogram and syndrome treatment are shown in Table 4. There was significant difference in appropriateness of vancomycin use in three group based on age (Neonate, Infant, Child) (P value= 0.017). The most appropriate use was in 29day-24 months (68.1%) and the least in 2-13 years (20%) (Table5). The main reasons of vancomycin administration were pneumonia (60 cases=59%) and sepsis (22cases=21.5%) in order, and other diagnosis as Table 6. All patients were given combination

therapy of vancomycin with one to five other antibiotics including Amikacin, Gentamicin, Ceftriaxon, Cefotaxim, Ceftazidim, Meropenem, Ampicillin, Piperacillin-Tazobactam, Clindamicin, Metronidazole. Final result of treatment based on appropriateness of vancomycin use is shown in table 7. Therapeutic monitoring of serum vancomycin concentrations was not available. There was no prophylactic use. No regimen was prescribed with pediatric infectious disease subspecialist consultation.

Discussion

The project work involves the drug utilization evaluation of vancomycin in a pediatric ward regarding diagnosis, culture results and host factors. In 102 studied patients, 46 males and 56 females received Vancomycin relatively equal in both as it is expected. Vancomycin has a narrow spectrum for special microorganisms with no sex predominance. All prescriptions were therapeutic. Only 6% had positive culture with 2% antibiogram. Near to total received vancomycin empirically, a finding more than commonly observed in other studies in adults in range of 69-79%^{7, 9-11}, and similar in pediatric as following studies. Saker reported vancomycin exposure rates for first evaluations of late-onset sepsis are high in very low birth weight infants as 60% based on having one or more positive blood cultures or receiving empiric vancomycin¹². Infections with organisms necessitating vancomycin treatment usually are serious and life-threatening diseases with very low to no chance waiting for

Table 1: Number and percent of patients receiving Vancomycin based on age.

Age	Number	Percent
0 – 28 Days	45	%44
29D-24 Month	47	%46
2 – 13 Year	10	%10
Total	102	%100

culture and antibiogram results. Prescriptions were usually based on syndrome diagnosis and epidemiologic factors. Appropriateness of vancomycin use based on culture with antibiogram and syndrome treatment were reversed but this cannot be relied because of low number of cultures. In our study Vancomycin was used appropriate in 58 cases (57%) based on CDC, ASHP and IDSA guidelines and inappropriate in 44 cases (43%) in pediatric ward. In Oliveira study out of 118 vancomycin prescriptions, 95 (80.5%) were considered appropriate. Appropriate use was based on empiric therapy with risk factors, treatment of proven Gram-positive infections and Beta-lactam allergy; inappropriate use was based on empiric therapy without risk factors and continued empiric use without further evidence of Gram-positive infection in pediatric and adult patients overall without separating and analyzing¹³. An evaluation of antibiotic prescription pattern based on DDD counting showed high use of essential drugs of vancomycin and imipenem by defined daily dose calculation in patients 0.5 to 96 years. This was partly due to type of patient's disease (heart surgery) and partly due to lack of sufficient knowledge about common antibiotic

Table 2: Diagnostic Methods used in patients receiving Vancomycin.

Diagnostic Method	Number	Percent
Clinical	13	12.7
Clinical + Culture	5	4.9
Clinical + Radiology	81	79.4
Clinical + Radiology + Sonography	2	2
Clinical + Culture + Radiology + Sonography + CT Scan	1	1
Total	102	100

Table 3: Number and percent of appropriate and inappropriate use of Vancomycin based on studied factors.

Appropriateness	Number	Percent
A	58	56.9
B	44	43.1
B1	14	13.7
B2	0	0
B3	0	0
B4	0	0
B5-1	0	0
B5-2	2	2
B5-3	3	2.9
B5-4	1	1
B6-1	0	0
B6-2	0	0
B7	9	8.8
B8-1	7	6.9
B8-2	1	1
B5-2, B5-3, B7	3	2.9
B7, B8-2	2	2
B5-3, B7	1	1
B5-2, B1	1	1
Total	102	100

B1:Unnecessary, B2:Age, B3:Concomitant Disease, B4:Insufficient Spectrum, B5-1:Low Broad Spectrum, B5-2:High Broad Spectrum, B5-3:Unnecessary Combination of Two Similar Spectrum Antibiotic, B5-4:Ineffective, B6-1:Low Dose, B6-2: High Dose, B7:Improper Combination, B8-1: Short Duration, B8-2:Long Duration

resistance objects in hospital¹⁴. Al Za'abi from Oman

reported 79.1 % inappropriate use of vancomycin based on HICPAC guidelines in adult and pediatric patients. This was mainly due to the continuous use of vancomycin following negative microbiological cultures for β -lactam-resistant Gram-positive microorganisms. Therapeutic drug monitoring (TDM) practices did not comply with recommendations on the use of trough concentration in the specified range as a guide for monitoring of therapy¹⁵.

In this study there was inappropriate indication and unnecessary use in 14% of cases. Fahimi study in one year showed inappropriate indication and dosing regimen of vancomycin in 97.7% of adult and pediatric cases. The most use of vancomycin was recorded in hematology – oncology ward mostly as empirical and Intensive Care Unit (ICU). Culture responses were negative despite great clinical evidence of infection¹⁶. In Salehifar study considering the indication, Vancomycin was administered appropriately in 58 percent of adult patients⁹. In Wendy study, utilization of vancomycin was appropriate in 98% of patients in a Pediatric Emergency Department based on admitting diagnosis¹⁷. A retrospective drug utilization evaluation in pediatric patients who received intravenous vancomycin, 64.6% and 89.6% courses were consistent with guidelines for indication of therapy and dosing regimen in order¹⁸. Megan Bollinger reported four main reasons of inappropriate use of vancomycin in patients 8 days to 93 years including below-target dosing, short duration of use, inadequate monitoring of serum trough levels (72% sub therapeutic serum levels) and low blood cultures done (65.6% of cases)¹⁹.

In Askarian study in Shiraz on both children and adult, of the 200 patients, 92% were prescribed the appropriate vancomycin dose and 51.5% received the appropriate duration of treatment. In 6.0% of the patients the prescription of vancomycin was appropriate according to HICPAC guidelines²⁰. In this

Table 4: Number and percent of appropriate and inappropriate use of Vancomycin based on Antibigram.

Appropriateness	Appropriate		Inappropriate		Total	
	No	Percent	No	Percent	No	Percent
With Antibigram	2	1.9%	4	4.1%	6	6%
Without Antibigram	56	55%	40	39%	96	94%
Total	58	56.9%	44	43.1%	102	10%

Table 5: Number and percent of appropriate and inappropriate use of Vancomycin based on age.

Appropriateness Age	Appropriate		Inappropriate		Total	
	Number	Percent	Number	Percent	Number	Percent
1 – 28 day	24	53.3	21	46.7	45	100
29day - 24 Month	32	68.1	15	31.9	47	100
2 – 13 Year	2	20	8	80	10	100
Total	58	56.9	44	43.1	102	100

Table 6: Number and percent of appropriate and inappropriate use of Vancomycin based on diagnosis.

Appropriateness Diagnosis	Appropriate		Inappropriate	
	No	%	No	%
Pneumonia	39	65	21	35
Unknown Origin Sepsis	11	50	11	50
UTI	0	0	3	100
Meningitis	0	0	1	100
Gastroenteritis	0	0	2	100
Bronchiolitis	1	50	1	50
Lymphadenopathy	2	100	0	0
BPD ¹	0	0	1	100
Umbilical Cord Inf.	1	50	1	50
NEC ² , Premature	1	100	0	0
Intestinal Atresia	1	100	0	0
Asthma	0	0	1	100
Shigellosis	0	0	1	100
Hirschsprung's disease	1	100	0	0
Sickle Cell Anemia	0	0	1	100
Metabolic Dis.	1	100	0	0
Total	58	56.9	44	43.1

¹BPD: Bronchopulmonary Dysplasia, ²NEC: Necrotizing Enterocolitis

study the most common reason of inappropriate use was unnecessary use in 13.7% followed by improper combination, short duration, as 8.8%, 6.9% in order, incorrect combination of two similar spectrum antibiotic, concurrent high broad spectrum, ineffective, long duration and insufficient spectrum each in 1- 3% of cases and totally in 6 to 14% different combination of errors. Overall irrational use of vancomycin is due to high consumption with different errors. Many studies measured antibiotics usage with DDDs number. This is a DUE of Vancomycin regarding host factors. There was no fault in prescribing related to weight and renal function and no contraindication of starting and continuing vancomycin by drug side effect as thrombocytopenia and others. Appropriateness of drug administration cannot be compared based on diagnosis because of unequal number of diseases. Outcome was 1.5 to 2 times better in appropriate than

inappropriate use. Therapeutic monitoring of serum vancomycin concentrations was not available which may cause missing sub therapeutic levels of the drug and usefulness. A very low positive culture also is an important factor in improper prescription of the drug.

Conclusion

Drug utilization evaluation is best criterion for assessing the clinical appropriateness and effective use of a drug. Rational use of antibiotics lowers emergence of resistance. These results showed the need to strengthen measures of drug use control. No restriction policy is suggested. Improving microbiologic cultures, investigation of Vancomycin serum levels and simultaneous continued medical education for antimicrobial decisions hence would lower empirical and raise rational use rate.

Table 7: Final result of treatment based on appropriateness of vancomycin use.

Result	Appropriateness		Inappropriate		Total	
	No	%	NO	%	NO	%
Improvement	47	59.5	32	40.5	79	100
No Improvement With Changing Antibiotics After 48 – 72 hours	1	33.3	2	66.7	3	100
No Improvement Without Changing Antibiotics After 48 – 72 hours	3	30	7	70	10	100
No Improvement with Antibiogram	0	0	1	100	1	100
No Improvement and DAMA ¹	4	80	1	20	5	100
No Improvement and refer to other center	1	100	0	0	1	100
Death	2	66.7	1	33.3	3	100

¹ DAMA: Discharge against Medical Advice

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