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Drug Utilization Evaluation Of Vancomycin In Teaching Hospitals Of Lahore

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ABSTRACT:

Vancomycin is the drug of choice in treating severe Gram-positive infections. Drug utilization evaluation is an effective method to promote interventions that will endorse patient outcomes and cost-effectiveness of the drug therapy. The objective of the study undertaken was to observe the utilization of vancomycin in different teaching hospitals of Lahore. A data collection form was designed and distributed among the healthcare providers gathering information about its prescribing pattern. It was found that vancomycin was being used rationally yet special precautions should be followed. The brand Vancomycin (76%) was used in majority of the hospitals. 96% of the prescribers was well aware of its antibacterial spectrum. According to 68% of prescribers the therapy was cost-effective. Redman's syndrome was reported in 44% of the cases. This study concludes that vancomycin is being used appropriately in right doses and for right indications and is cost effective to the majority of patients.

Key Words: Cost-effectiveness, Evaluation, Patient Outcomes, Rational, Utilization.

INTRODUCTION:

Drug utilization evaluation is an effective mechanism to identify individual variability in drug use and to promote interventions that will improve positive patient outcomes [1]. DUR is an ongoing, systematic course designed to uphold the appropriate and effective use of medications [2]. It involves a comprehensive and ample review of a patient's medication and health history before, during, and after dispensing in order to attempt to achieve appropriate therapeutic decision-making and positive patient outcomes. Pharmacists participating in DUR programs can directly improve the quality of care for patients, individually and as populations, by striving to prevent the use of redundant or inappropriate drug therapy, prevent adverse drug reactions and improve overall drug effectiveness. Other terms considered synonymous with DUR include drug use evaluation (DUE), medication use evaluation (MUE), and medication use management. American Society of Health System Pharmacists (ASHP) currently espouses the nomenclature medication use evaluation (MUE) [3].

Vancomycin is a glycopeptide antibiotic used to treat severe gram-positive infections caused by organisms that are resistant to other antibiotics such as methicillin-resistant staphylococci and ampicillin-resistant enterococci. It is administered by intravenous infusion. It never became first-line treatment for *Staphylococcus aureus* for plentiful reasons; it must be given intravenously for most infections because of its poor oral bioavailability. β -lactamase-resistant semi-synthetic penicillins such as methicillin (and its successors, nafcillin and cloxacillin) were subsequently developed, which have better activity against non-MRSA staphylococci [4]. Vancomycin shows its effects by inhibiting proper cell wall synthesis in Gram-positive bacteria. It is poorly absorbed when administered by mouth and for systemic infections it must be given intravenously. Since the drug is excreted chiefly via the kidneys, dosage modification is imperative in patients with impaired renal function. It is considered that excessively high serum concentrations of vancomycin may be associated with ototoxicity. So far it has not been possible to relate the development of nephrotoxicity to previously determined serum concentrations of vancomycin [5].

Vancomycin is indicated for the treatment of severe, life-threatening infections by Gram-positive bacteria that are unresponsive to other less-toxic antibiotics. In particular, vancomycin should not be used to treat methicillin-sensitive *Staphylococcus aureus* because it is inferior in action to penicillins such as nafcillin [6] [7].

The mounting emergence of vancomycin-resistant enterococci has resulted in the development of guidelines for use by the Centers for Disease Control (CDC) Hospital Infection Control Practices Advisory Committee. These guidelines restrict use of vancomycin to the following indications; [8] [9] serious infections caused by susceptible organisms resistant to penicillins or in individuals with severe allergy to penicillins, pseudomembranous colitis caused by the bacterium Clostridium difficile, infections caused by gram-positive microorganisms in patients with serious allergies to beta-lactam antimicrobials, antibacterial prophylaxis for endocarditis following certain intervening procedures, surgical prophylaxis for major procedures involving implantation of prostheses, early in treatment as an empiric antibiotic to cover for possible MRSA infection while waiting for culture identification of the infecting organism [9].

The common adverse drug reactions associated with vancomycin therapy include: local pain, which may be severe and/or thrombophlebitis after IV administration, nephrotoxicity and ototoxicity [10] [11]. Rarely occuring adverse effects include: anaphylaxis, toxic epidermal necrolysis, erythema multiforme, red man syndrome, superinfection, thrombocytopenia, neutropenia, leucopenia, tinnitus, dizziness and/or ototoxicity [8]. It has recently been emphasized that vancomycin can stimulate platelet-reactive antibodies in the patient, leading to severe thrombocytopenia and bleeding with florid petechial hemorrhages, ecchymoses, and wet purpura [12].

Acquired microbial resistance to vancomycin is a rising problem, in particular, within healthcare facilities such as hospitals. With vancomycin as the last-line antibiotic for serious Gram-positive infections, there is the growing prospect that resistance may result in a return to the days when fatal bacterial infections were common. Vancomycin-resistant Enterococcus (VRE) emerged in 1987. Vancomycin resistance appeared in more common pathogenic organisms during the 1990s and 2000s, including vancomycin-intermediate *Staphylococcus aureus* (VISA), vancomycin-resistant *Staphylococcus aureus* (VRSA)and vancomycin-resistant *Clostridium difficile* [13] [14]. There is some suspicion that agricultural use of avoparcin, a similar glycopeptide antibiotic, has contributed to the emergence of vancomycin-resistant organisms. Three main resistance variants have been illustrated to date among resistant *Enterococcus faecium* and *E. faecalis* populations; Van A - resistance to vancomycin and teicoplanin; inducible on exposure to these agents, Van B - lower-level resistance; inducible by vancomycin, but strains may remain susceptible to teicoplanin and Van C - least clinically important; resistance only to vancomycin; constitutive resistance. The development and usage of novel antibiotics such as linezolid and daptomycin are expected to delay, but not halt, the emergence of bacterial resistant to all accessible antibiotics.

Antibiotic resistance to all the conventionally used antibiotics is ever increasing. All the strains are susceptible to Linezolid which is an expensive alternative with adverse effects. If resistance to Linezolid appears then Quinupristin with Dalfopristin are the drugs of choice. Judicious and careful use of antibiotics focuses on the compliance and formation of antibiotic policy guide lines is highly recommended.

MATERIALS AND METHODS:

A retrospective study was carried out to evaluate the utilization of vancomycin. It was carried out at five different teaching hospitals in Lahore i.e., A, B, C, D and E. Around 50 healthcare providers (physicians, pharmacist, nurses and other allied healthcare professionals) were randomly selected and interviewed. Information about prescribing pattern of medicine such as indications, pharmacokinetics, adverse effects, resistance to the therapy, cost effectiveness, etc. was obtained. The significant and relevant information was integrated on a predesigned Performa. The data collection form developed for drug utilization evaluation contained questions related to physician's awareness about the drug; brand, dosage form, side effects, resistance, etc. The duration of study was one month.

Inclusion criteria:
Health care providers including physicians, pharmacists, staff nurses, paramedical staff, allied healthcare professionals, etc. were included in the study.

Exclusion criteria:
The exclusion criteria were not specific.

RESULTS AND DISCUSSION:

Vancomycin is the drug of choice for Gram-positive bacterial infections. It is used in the treatment of serious infections caused by susceptible organisms resistant to penicillins (MRSA and MRSE) or in individuals with serious allergy to penicillins, pseudomembranous colitis, peritonitis, endocarditis, etc.

The project work involves the drug utilization review of vancomycin, a study of prescriptions to evaluate appropriateness and cost-effectiveness of the therapy. A total of 50 health care professionals were interviewed about vancomycin's prescribing in five different teaching hospitals. The brand of vancomycin most commonly being used is Vancomycin i.e. 76% (Fig. 1). It is mostly used for the treatment rather than prophylaxis, therefore serves a major use in majority of the hospital settings. Most of the prescribers have appropriate knowledge regarding vancomycin's prescribing as it is being given for the right indications (mostly for endocarditis) and in right doses (Fig. 2). A lesser portion of prescribers are prescribing vanomycin in subtherapeutic doses. The dosing frequency is appropriate i.e. 8 hourly or 12 hourly.

Vancomycin has poor oral absorption. Hence the dosage form mostly being used is injection. 68% of the prescribers reckon that the therapy is cost effective which exhibits that vancomycin is being used appropriately (Fig. 3). Redman syndrome is the most common adverse effect occurring with vancomycin therapy (Fig. 4). If due care is given on the infusion time i.e. 15-30 minutes, this adverse effect can be avoided. But the staff nurses are in hurry due to workload and the innate nature of humans of being in hurry; they administer the drug rapidly, which results in flushing of the whole upper body of patient. Tinnitus, renal impairment, etc are also encountered. As the therapeutic index of vancomycin is low so the plasma drug levels must be monitored. Half of the prescribers held that the therapy is discontinued after tinnitus while others were naive about discontinuation of therapy. A satisfactory percentage (36%) of

prescribers quoted that no adverse effects are being observed with the therapy. According to 24% of prescribers, toxicity reactions are seen with vancomycin therapy (Fig. 5)

Prescribers have sufficient knowledge regarding the antibacterial spectrum of vancomycin hence it avoids unnecessary prescribing. It is rarely prescribed for off-label uses, which also contributes to the effective therapy (Fig. 6).

In majority of the hospitals vancomycin is under the Monitored category of the formulary. Few have it under Conditional category. The rational practice is that vancomycin should not be prescribed orally for systemic infections. According to 68% of prescribers, they are not prescribing vancomycin orally for systemic infections.

Acquired microbial resistance to vancomycin is a growing problem, in particular, within healthcare facilities such as hospitals (Fig. 7). With vancomycin as the last-line antibiotic for serious Gram-positive infections, there is the growing prospect that resistance will result in a return to the days when fatal bacterial infections were common. As in some rare cases vancomycin is given to Methicilin-sensitive Staphylococcus aureus infections, where it is totally absurd to prescribe it. Hence it is contributing to the increased resistance to vancomycin. The duration of therapy is not a contributing factor to the increased resistance as per the observation. Alternative drugs are present in case of resistance to vancomycin but unfortunately prescribers are not aware of the accurate prescribing after occurrence of resistance. Patients are taking OTC drugs along with the therapy. But due regard must be given to the possible interactions and pharmacist should intervene for consultation.

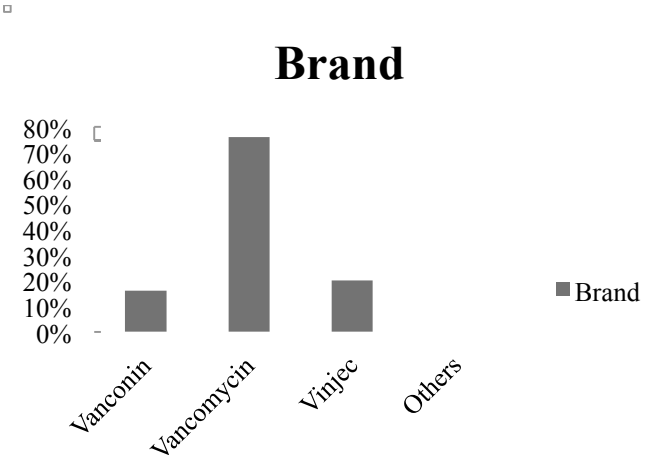
It is observed that the knowledge of healthcare providers is sufficient for appropriate vancomycin prescribing. The drug is being used rationally by majority of the prescribers in our healthcare system. There is incidence of adverse effects which cannot be avoided completely as no drug is completely safe. Drugs are only tools which show their affects when they come in contact with the biological system. Every drug is unique in its actions. As long as it is effective, the risk to benefit ratio is being considered and it is prescribed. The brands of vancomycin being used are appropriate and cost effective and have acceptable pharmacokinetics.

The effectiveness of vancomycin therapy can be enhanced and the adverse effects can be avoided to some extent by more vigilant n avid attitude of prescribers, nurses and other allied health professionals. It would require a more collaborative practice among physicians and pharmacists so that pharmacists can guide them about the rational prescribing and safer use of medicine. Pharmacists should also guide nurses on proper administration of vancomycin and provide consultation on the use of OTC drugs along with vancomycin. The ADR reporting system should be made efficient to avoid the incidence of adverse effects associated with the therapy. In our healthcare setup majority of the ADRs are unnoticed. Patients should be given sufficient information regarding their medicine so that they can identify any abnormal finding in their course of therapy.

Table-1. Brand of Vancomycin:

Brands	Number	Percentage
Vanconin	8	16%
Vancomycin	38	76%
Vinjec	10	20%
Others	0	0

Figure-1. Brand of Vancomycin:

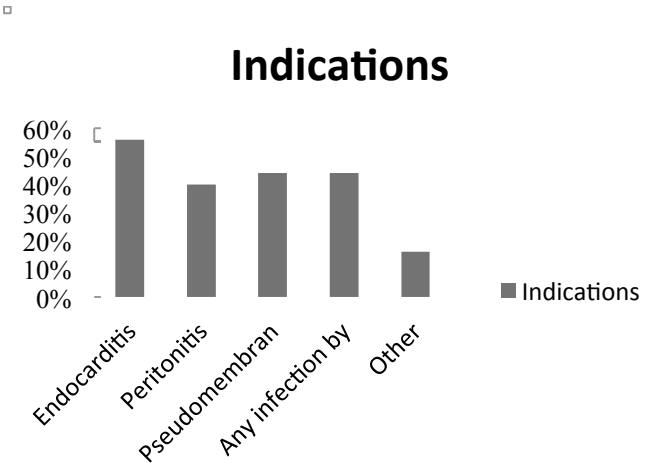


N=50: The brand Vancomycin is being used in majority of the hospitals accounting for 76%.

Table-2. Indications for Vancomycin:

Indications	Number	Percentage
Endocarditis	28	56%
Peritonitis	20	40%
Pseudomembranous colitis	22	44%
Any infection by Gram positive cocci	22	44%
Other	8	16%

Figure-2. Indications for Vancomycin:

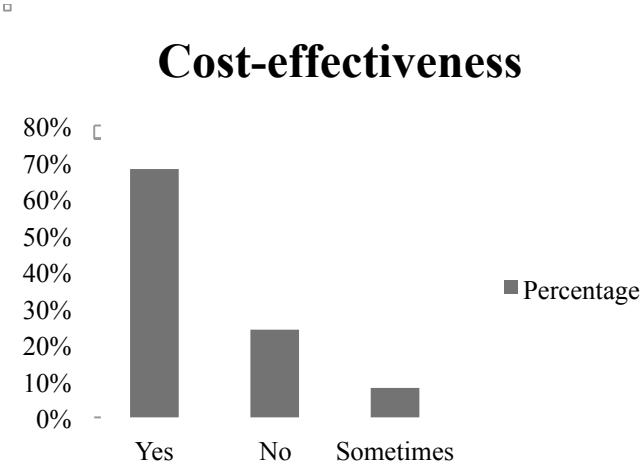


N=50: In 56% of cases vancomycin is used for endocarditis.

Table-3. Cost-effectiveness of Therapy:

Cost-effective	Number	Percentage
Yes	34	68%
No	12	24%
Sometimes	4	8%

Figure-3. Cost-effectiveness of Therapy:

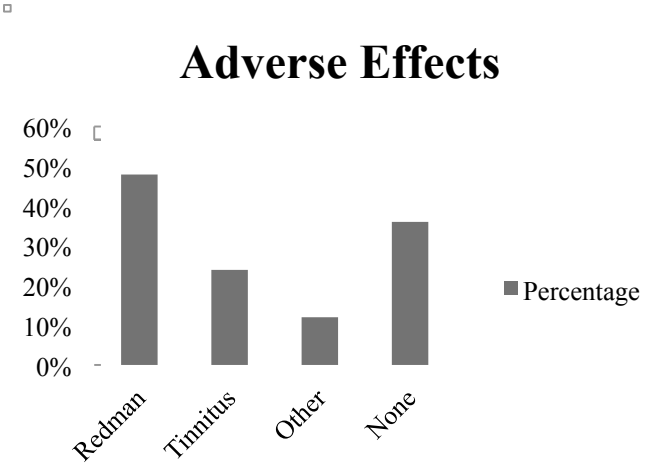


N= 50: According to the 68% of prescirbers the vancomycin therapy is cost-effective.

Table-4. Adverse effects:

Adverse Effects	Number	Percentage
Redman Syndrome	24	48%
Tinnitus	12	24%
Other	6	12%
None	18	36%

Figure-4. Adverse effects:

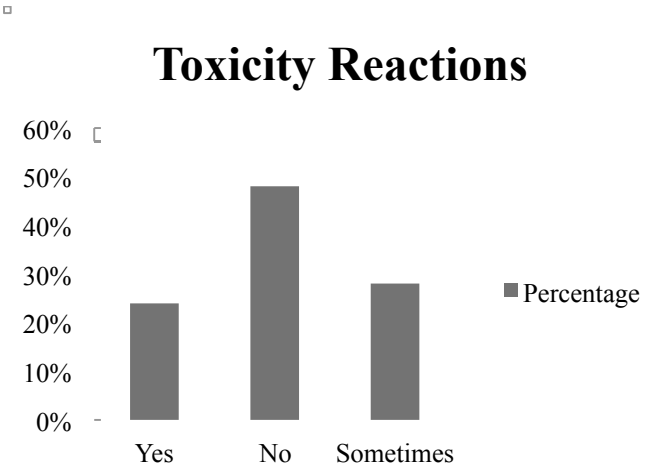


N= 50: The incidence of occurrence of Redman's syndrome is 48%.

Table-5. Toxicity reactions with Vancomycin therapy:

Toxicity Reactions	Number	Percentage
Yes	12	24%
No	24	48%
Sometimes	14	28%

Figure-5. Toxicity reactions with Vancomycin therapy:

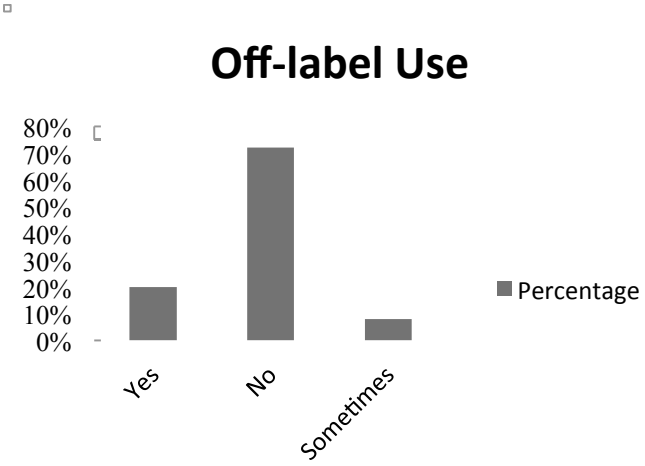


N=50: Toxicity reactions are seen only in 24% of cases.

Table-6. Prescribed for Off-label Uses:

Prescribed	Number	Percentage
Yes	10	20%
No	36	72%
Sometimes	4	8%

Figure-6. Prescribed for Off-label Uses:

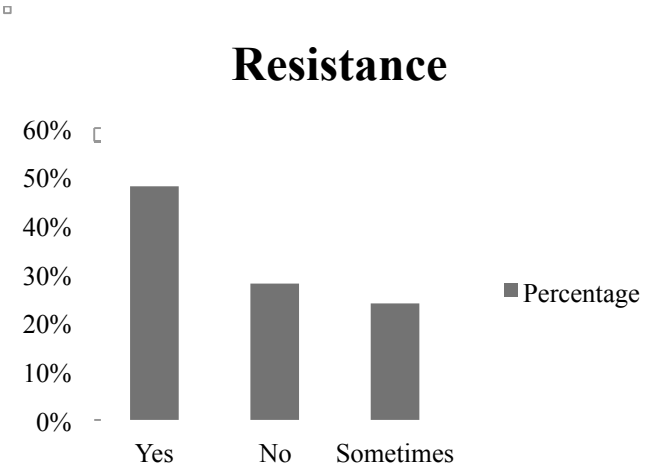


N= 50: In 72% of cases vancomycin is not prescribed for off-label uses.

Table-7. Resistance in Bacterial Infections:

Resistance	Number	Percentage
Yes	24	48%
No	14	28%
Sometimes	12	24%

Figure-7. Resistance in Bacterial Infections:



N= 50: In 48% of the cases resistance is seen in bacterial infections with vancomycin.

CONCLUSION:

Drug utilization and evaluation is best criterion for assessing the clinical appropriateness, cost effectiveness and effective use of a drug therapy. The study conducted shows that vancomycin is the drug of choice for Gram-positive bacterial infections and is being used, in majority of the public sector teaching hospitals, with all its clinical significance. It is being used rationally in the treatment of serious infections caused by susceptible organisms resistant to penicillins (MRSA and MRSE) or in individuals with serious allergy to penicillins, pseudomembranous colitis, peritonitis, endocarditis, etc. Vancomycin therapy proves to be cost effective. Its off-label use is prohibited in many hospitals. Proper dose, dosage form and duration of therapy are being followed which lead to effective and rational use of vancomycin. Acquired resistance to vancomycin therapy is becoming common. The doses and duration of therapy should be carefully prescribed to avoid the occurrence of resistance in bacterial infections. Special precautions are not being followed in many cases. More emphasis should be given on it. Vancomycin has certain side effects, as every other drug, but they can be minimized under vigilant supervision of a pharmacist. ADR reporting system should be made efficient to avoid such events in future.

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