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Clinical Pharmacology of Vancomycin in Pediatrics

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Abstract

Vancomycin plays an indispensable therapeutic function in managing severe infections caused by MRSA in the children population. Preponderance children dosing references for vancomycin recommend a daily dose of 40 mg/kg/day for empirical treatment, while a dose of 60 mg/kg/day is recommended for CNS infections. Vancomycin is absorbed in fewer amounts through PO in GIT, it is thus IV administered. IV infusions of vancomycin perhaps cause pain, phlebitis, erythema, urticaria, flushing, hypotension, tachycardia and the red man syndrome. Coincident administration of vancomycin with amphotericin-B, NSAIDs, aminoglycosides, cisplatin and other nephrotoxic agents perhaps exaggerated the risk of nephrotoxicity. Concomitant administration of vancomycin and furosemide, aminoglycosides, ethacrynic acid, etc perhaps increase the risk of ototoxicity. Coadministration of vancomycin and vecuronium increases the risk of neuromuscular blockage. If vancomycin and zidovudine are administered together, they increase the risk of neutropenia.

Keywords: *Clinical; Vancomycin; Pediatrics; Pharmacology.*

Introduction

Vancomycin is a glycopeptide antibiotic which has a narrow spectrum of activity directed to fight Gram- (+) microorganisms. Vancomycin has become a ubiquitously used medicine in hospital settings, where the occurrence of resistant Gram-(+) organisms is prevalent [1]. Vancomycin plays an indispensable therapeutic function in managing severe infections caused by MRSA in the children population. Recently, vancomycin is specifically considered a 1st-line medicine for empirical treatment, and also used as the medicine-of-choice in severe infections caused by MRSA [2]. Vancomycin has bactericidal activity depending on the concentration [3]. Vancomycin is particularly prescribed to fight severe infections caused by Gram-(+) bacteria, to combat microorganisms that are resistant to different antibiotic medications or still described to patients who are allergic to PCNs and cephalosporins [4,5]. Preponderance children dosing references for vancomycin recommend a daily dose of 40 mg/kg/day for empirical treatment, while a dose of 60 mg/kg/day is recommended for CNS infections. In adults, the recommended daily dose is 1 g every twelve hrs and the recommended trough level is 5 to 10 mg/L or 5 to 15 mg/ L [6]. The Infectious Diseases Society of America guidelines recommend vancomycin dosing of 15 mg/kg every six hrs or 60 mg/kg/day for children patients with severe infection. However, these dosing recommendations can influence to subtherapeutic trough concentrations and doses of 70 to 85 mg/kg/day necessitated to a target vancomycin serum trough concentrations of 15 to 20 mg/L [7-9]. Vancomycin is the medicine of choice for the management of Gram-(+) bacterial infections caused by MRSA [10]. Despite shortcomings involving meager tissue penetration (specifically in the lung), relatively gradual bacterial killing, and it is potential for toxicity; vancomycin is regarded as the gold-standard for antibiotic treatment of MRSA infections owing to its less cost and settled clinical reaction [11].

Literature review

Pharmacokinetics

Vancomycin is absorbed in fewer amounts through PO in GIT, it is thus IV administered. In adults, a single IV dose of 1 g generates plasma concentrations of 15 to 30µg/ml one hr after a 1- to 2-hr infusion. It's absorption onto tissues is different and

frequently meager, in section related to its comparatively large size. The redistribution phenomenon in vancomycin concentrations made the analysis of peak plasma concentration of the medicine of further sophisticated, as there is a different coinciding to the individual's age. Vancomycin is nearly exclude to be eliminated renally, chiefly via glomerular filtration and certain active tubular secretion, so renal dysfunction also influences vancomycin degrees [12]. The medicine is eliminated by renal excretion, and only five percent of the medicine is metabolized. Nearly ninety percent of the administered dose is excreted by GFR. Its plasmatic t1/2 ranges from four to eleven hrs, with a mean of six hrs in patients with normal renal work. In case of renal impairment, the t1/2 is approximately seven days [13]. Because eighty percent–ninety percent of vancomycin is cleared through the kidneys, the t1/2 of the medicine in a patient's body depending heavily on renal functions [14-16]. Vancomycin shows complex PKs, with time-dependent bactericidal consequence and moderate post-antimicrobial outcome. It also has meager tissue penetration. The Vd in children less than 28 days is increased and the CL decreased, influencing to the potential for an increased t1/2 for the medication [17].

Mechanism of actions

Vancomycin inhibits bacterial cell wall generation by suppressing elongation of peptidoglycan & cross linking/ Vancomycin blocks transpeptidation by binding to D-alanyl-D-alanine residues of the bacterial cell wall [18].

Indication

Current guidelines recommend serum trough concentrations be maintained above 10 mg/L to avoid resistance, and to target 15 to 20 mg/L in complicated infections (e.g., bacteremia, endocarditis, osteomyelitis, meningitis, and hospital-acquired pneumonia antecedent by S. aureus [19]. Vancomycin, an antimicrobial described for MRSA infections, is ubiquitously used for severe infections such as meningitis, osteomyelitis, endocarditis, bacteremia, hospital acquired pneumonia, and serious skin and soft tissue infection [19]. Trough concentrations of 10-15 mg/L are desired for entirely different infections, as serum concentrations < 10>

Skin and soft tissue infections

Skin abscesses, cellulitis, myositis, and fasciitis are often antecedent by MRSA, and perhaps require vancomycin coverage, at least until clinical improvement (and potentially surgical intervention) has happened [20].

Bone and joint infections

Vancomycin is most frequently used in this setting for the management of MRSA pyogenic arthritis and osteomyelitis [21].

Bacteremia

MRSA perhaps a cause of bacteremia in immuno-competent hosts without indwelling central venous lines [20].

Central nervous system infections

Vancomycin perhaps necessitated for coverage of Gram (+) infections of the CNS [22].

Pulmonary infections

MRSA perhaps cause pneumonia (either community acquired or nosocomial and ventilator consociated). High doses of vancomycin and higher degree perhaps necessitated, bestowed the potential severity of MRSA pneumonia and the meager and different penetration of vancomycin into lung tissues [23].

Adverse drug reaction

vAKI is a ubiquitously reported adverse drug reaction in children patients taking treatment with vancomycin [24-26]. Hypersensitivity reaction such as urticaria, exfoliative dermatitis, macular rashes, eosinophilia, vasculitis, transient anaphylaxis, and, sometimes, vascular collapse Stevens-Johnson syndrome, Toxic epidermal necrolysis, macular cutaneous rashes (e maculopapular exanthema, are described by itchy or non-itchy spreading lesions that perhaps launch on the trunk and upper limbs) and anaphylaxis, including hypotension, dyspnea, urticaria or itching [27,28]. IV infusions perhaps cause pain, phlebitis, erythema, urticaria, flushing, hypotension, tachycardia and the red man syndrome. The red man syndrome is described by the onset of intense redness over the upper part of the body ("red neck") or painful trunk muscle spasms [21]. Thrombophlebitis which perhaps associated with chills, exanthema and fever is also an event related to vancomycin infusion [29]. Ototoxicity (direct injuries caused by the medicine to the auditory branch of the 8th cranial nerve), Vertigo, dizziness and tinnitus are perhaps rare side effects of vancomycin [4, 28]. Nephrotoxicity (poison to the kidney) is the potential adverse effects of vancomycin [30].

Contraindicated

Vancomycin is contraindicated in patients who had previous history of hypersensitivity to this antimicrobial. Solutions containing dextrose perhaps

contraindicated in patients with known allergy to corn or corn products. For those who had history of impaired hearing because vestibular injury and cochlear injury is consociated with tinnitus and senorineural hearing loss has been reported in humans after administration of vancomycin. IM administration because vancomycin cause the risk of necrosis at the site of administration.

2.6. Drug interaction: The combination of vancomycin and an aminoglycoside acts synergistically in vitro fight multiple strains of S. aureus, S. bovis, enterococci, and the viridans group streptococci. Coincidentally administration of vancomycin and anesthetic agents has been associated with erythema and histamine-like flushing and anaphylactoid reactions [31,32]. Coincident administration of vancomycin with amphotericin-B, NSAIDs, aminoglycosides, cisplatin and other nephrotoxic agents perhaps exaggerated the risk of nephrotoxicity. Concomitant administration of vancomycin and furosemide, aminoglycosides, ethacrynic acid, etc perhaps increase the risk of ototoxicity. Coadministration of vancomycin and vecuronium increases the risk of neuromuscular blockage. If vancomycin and zidovudine are administered together, they increase the risk of neutropenia. If vancomycin administered with dopamine or dobutamine, it decrease the vancomycin serum level [33].

Conclusion

Vancomycin has become a ubiquitously used medicine in hospital settings, where the occurrence of resistant Gram- (+) organisms is prevalent. Preponderance children dosing references for vancomycin recommend a daily dose of 40 mg/kg/day for empirical treatment, while a dose of 60 mg/kg/day is recommended for CNS infections. The medicine is eliminated by renal excretion, and only five percent of the medicine is metabolized. Coincident administration of vancomycin with amphotericin-B, NSAIDs, aminoglycosides, cisplatin and other nephrotoxic agents perhaps exaggerated the risk of nephrotoxicity. Concomitant administration of vancomycin and furosemide, aminoglycosides, ethacrynic acid, etc perhaps increase the risk of ototoxicity. Coadministration of vancomycin and vecuronium increases the risk of neuromuscular blockage. If vancomycin and zidovudine are administered together, they increase the risk of neutropenia.

Abbreviations

AUC: Area under the concentration–time curve; CNS: Central nervous system; Cmax: Maximum concentration; GFR: glomerular filtration rate; IM: Intramuscular; IV: Intravenous; Ke: elimination rate constant; MIC: Minimum inhibitory concentration; MRSA: Methicillin-resistant Staphylococcus aureus; Pgp: P-glycoprotein; SSTIs: Skin and Soft Tissue Infections; T1/2: Half-life; VAKI: Vancomycin associated acute kidney injury; VISA: Vancomycin-intermediate Staphylococcus aureus; Vd: Volume of distribution;

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