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ISSN: 2576-389X
Journal of Infectious Diseases and Diagnosis

Perspective

Impact of Therapeutic Drug Monitoring and Vancomycin Pharmacokinetics in Patients

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ABOUT THE STUDY

Vancomycin therapeutic drug monitoring is widely recommended for clinical treatment. However, few studies have been conducted to assess Vancomycin (VCM) pharmacokinetics in patients with abdominal cancer who are also suffering from severe infectious disease. The purpose of this study was to address the issues raised above and to find clinically useful information to predict and estimate the appropriate vancomycin dosage. For the first time, this study clearly demonstrated changes in the pharmacokinetic profile of vancomycin in abdominal cancer patients complicated by severe infectious disease [1]. The conclusion is that the initial vancomycin trough concentrations in these patients are significantly lower. We also discovered that Cys-C was linked to target trough achievement. As a result, the traditional standard vancomycin dose may put patients at risk of failing to achieve the recommended standard vancomycin trough concentrations. This finding emphasizes the importance of developing useful guidelines for vancomycin dosage individualization in abdominal cancer patients with severe infectious disease.

Previous research has shown that malignant tumors, as well as changes in volume of distribution due to edoema, peritoneum, or pleural effusion, can affect VCM PKs. Using the 2-compartment Bayesian PK approach they reported an increase in VCM Clearance (CL) in pediatric cancer patients, which was also confirmed in adult hematological malignancies [2]. The estimated VCM clearance between cancer patients and non-cancer patients did not significantly differ, according to opposing views, which suggests that dosage should only be adjusted by normal TDM. Nevertheless, it was hypothesized that cytokines like TNF-, which did indeed rise in the context of cancer *in vivo* tests, directly activated the renal organic anion/cation transporters (OCT1/2, OATs). Systemic inflammatory response syndrome usually developed in conjunction with Severe Infectious Illness (SIRS) [3]. This inflammatory reaction causes capillary leakage, vasodilatation, and the emergence of a hyper dynamic cardiovascular state with third-space, a high cardiac output, and increased blood flow to the major tissues and organs.

Vancomycin is mostly eliminated by the kidneys since it is water soluble. Increased renal blood flow, which improves vancomycin clearance through urine and lowers plasma vancomycin concentration, is very likely the cause of increased CL. Additionally, increased Volume of distribution (Vd) is typically attributable to SIRS-induced third space, which causes marked over hydration. But more research is still needed to understand the fundamental process that raises vancomycin CL and Vd levels. It has recently been suggested to use the term "Augmented Renal Clearance" (ARC) to refer to the increased renal elimination of circulating solutes seen in critically unwell individuals. The majority of researches have demonstrated that hyper dynamic circulation is characterized by elevated renal blood flow, with an elevated glomerular filtration rate as a probable cause. However, no data were provided on the number of oncological patients included in these investigations. Age, sepsis, and SIRS are risk factors for ARC, according to a previous study. Therefore, ARC rather than oncological status was most likely linked to the higher vancomycin CL found in this investigation. They had the opinion that cancer status could possibly contribute to ARC occurrence.

This opinion should be considered cautiously because the study is simply a case report. There is no guideline for this treatment in actual practice, and clinical research in China has not treated ARC seriously. Even though dose adjustment is permitted at the clinician's discretion and the results of the therapeutic drug monitoring showed very low concentrations, they typically do not give the idea any thought. Only a small number of these 78 patients met the target level. The standard vancomycin dose recommended in the package instructions approved by Chinese authorities appears to be too low in clinical practice to achieve the target trough concentrations. This result could be explained by the fact that the standard vancomycin administration algorithm was developed using data from relatively healthy patients. Furthermore, our research strongly suggests that

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Received: 04-Jul-2022, Manuscript No. JIDD-22-17770 ; **Editor assigned:** 06-Jul-2022, PreQC No. JIDD-22-17770 (PQ) ; **Reviewed:** 20-Jul-2022, QC No JIDD-22-17770; **Revised:** 27-Jul-2022, Manuscript No. JIDD-22-17770 (R) ; **Published:** 03-Aug-2022, DOI: 10.35248/2576-389X.22.07.178

Citation: Suzuki T (2022) Impact of Therapeutic Drug Monitoring and Vancomycin Pharmacokinetics in Patients. J Infect Dis Diagn. 7:178.

patients with abdominal cancer require higher dose regimens [4]. In this study, we discovered a strong relationship between vancomycin trough concentrations and age, body weight, serum creatinine, and, most importantly, Cystatin C (Cys-C). For the first time in patients with abdominal cancer, this study confirmed the relationship between Cys-C and vancomycin trough concentrations. Cys-C is a low molecular weight, non-glycosylated basic protein with 120 amino acids. Human Cys-C is a house keeping gene that is produced stably by all human nucleated cells. In previous studies, Cys-C was found to be age, muscle mass, and body mass index independent in healthy individuals.

Although previous research found a link between serum Cys-C levels and the progression of colorectal cancer, melanoma, and ovarian cancer, new research shows that Cys-C can be very effective in predicting renal function in cancer patients. These characteristics explain a portion of the relationship between Cys-C and vancomycin trough concentrations. This observational study was conducted in a live clinical practice. Because serum Cys-C levels are readily available in clinical practice, these parameters may enable physicians and/or pharmacists to predict vancomycin dose requirements in a short period of time. Identifying insufficient vancomycin trough concentrations earlier could be used to improve antimicrobial adequacy. An earlier achievement of the initial goal vancomycin trough concentration means a shorter duration of mechanical ventilation and a shorter duration of vasoactive agent, resulting in earlier hemodynamic stability. With this conclusion, clinicians should be able to confidently adjust vancomycin doses [5]. We need more research on specific dose adjustment algorithms. They recently confirmed that a vancomycin dosing algorithm based on estimated glomerular filtration rate from creatinine and Cys-C levels significantly improved goal trough achievement in ICU patients with stable kidney function compared to Cockcroft-Gault creatinine clearance.

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