Evaluation of Vancomycin Pharmacokinetic Model for Pediatric Cancer Population,

Sauvé Z[1]., Blouin M[1], Metras ME[1,2], Autmizguine J[3,4,5], Marsot A[1,5],

1. Faculty of Pharmacy, Université de Montreal, Canada
2. Department of Pharmacy, CHU Sainte Justine, Montréal, Canada
3. Department of Pharmacology and Pediatrics, Université de Montreal, Canada
4. Clinical Pharmacology Unit, CHU Sainte Justine, Montréal, Canada
5. Research center, CHU Sainte Justine, Montréal, Canada

Background

The 2020 vancomycin dosing recommendation using AUC/MIC as target stress the importance of an accurate pharmacokinetic model. There are few such models for pediatric cancer patients, a population especially vulnerable to the risk of inadequate concentration. The aim of this study was evaluate the vancomycin pharmacokinetic models currently described in the literature with data from local pediatric cancer patients.

Methods

A retrospective analysis was performed with the vancomycin concentrations data from pediatric cancer patients between January 2019 to January 2021 at the CHU Sainte Justine (Montreal, Canada). Patients received vancomycin by 1 hour infusion, four time daily, with dosage adapted according to therapeutic drug monitoring results. A literature review was performed to identify vancomycin models developed on pediatric oncology, oncology, and pediatric population. Predicted concentrations were derived using NONMEM(v7.5) , and bias and imprecision were derived for each model. If no model were acceptable (bias and imprecision respectively > ±15 % and >30%), re-estimation of model parameters (clearance or clearance and volume) was performed.

Results

This study included 108 patients (mean[SD] of age and weight respectively 7.68 [5.37] years and 32.8 [23.1] kg) , representing 566 vancomycin concentrations. Thirteen models were identified from the literature and tested with either fixed or estimated parameter. The model with the best overall performance was one-compartment with allometric weight effect on clearance and volume, and age effect on clearance, as described by He CY, with re-estimated values of clearance and volume of 3.94 L/h and 30.27 L, respectively. This model had a bias of -4.14% and an imprecision of 34.5%. Similarly acceptable models were (i) a re-estimation of model by Guilhaumou R (1-compartment model with weight and disease type effect on clearance) and (ii) the model by Okada (2-compartments model with creatinine clearance on clearance and bodyweight on volume), with a bias of respectively 5.57% and 6.77% and an imprecision of respectively 44.4% and 40.4%. Additionally, all models tend to overpredict low concentration values.

Conclusions

The relatively high imprecision of the models evaluated highlights the importance of external evaluation of models before clinical use, especially for specific sub-population.

Key Words

Vancomycin, Pediatric, Oncology