

A new algorithm optimized for initial dose settings of vancomycin using machine learning Imai S¹, Takekuma Y², Kashiwagi H¹, Miyai T³, Sugawara M^{1,2} 1. Faculty of Pharmaceutical Sciences, Hokkaido University, 2. Department of Pharmacy, Hokkaido University Hospital, 3. Graduate School of Life Science, Hokkaido University

Background: Generally, dose settings of drugs such as antibiotics are made on the basis of population pharmacokinetics (PPK) parameters. For example, in Japan, the initial dose settings of vancomycin (VCM) are determined using therapeutic drug monitoring analysis software that incorporates Japanese PPK parameters. On the other hand, there are no reports of applying machine learning (ML) to drug dose setting, although it is possible that ML can help achieve accurate drug dose settings. This study aimed to construct an optimal algorithm for initial dose settings of VCM using ML with decision tree (DT) analysis.

Methods: Patients who were administered intravenous VCM and underwent TDM at the Hokkaido University Hospital were enrolled. The study period was November 2011 to March 2019. In total, 654 patients were included in the study. Patients were divided into two groups, training (patients who received VCM from November 2011 to December 2017; n = 496) and testing (patients who received VCM from January 2018 to March 2019; n = 158) groups. For the training group, DT analysis of the classification and regression tree (CART) algorithm was performed to construct an algorithm (called DT algorithm) for the initial dose settings of VCM. For the testing group, the rates of attaining the VCM therapeutic range (trough value = 10–15 and 10–20 mg/L) with the DT algorithm and three conventional dose-setting methods were compared for model evaluation. The DT algorithm was constructed to be used for patients with estimated glomerular filtration rate ≥ 50 mL/min and body weight ≥ 40 kg.

Results: In the DT algorithm, the recommended daily doses ranged from 20.0 to 58.1 mg/kg. In model evaluation, the DT algorithm obtained the highest rates of attaining the VCM therapeutic range compared to conventional dose-setting methods.

Conclusions: Our DT algorithm has the potential to be applied to clinical practice. In addition, our study firstly indicated the usefulness of ML for drug dose setting.

Keywords: machine learning; decision tree analysis; vancomycin; therapeutic drug monitoring