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Perspective

Vancomycin Pharmacodynamics and Pharmacokinetics in Severe COVID-19 Patients

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DESCRIPTION

Coronavirus disease (COVID-19) has been rapidly spreading over the world since December 2019, with nearly 3 million verified cases and 204 thousand fatalities by April 29, 2020. 50% of non-survivors and 31% of patients who needed invasive mechanical ventilation both had secondary bacterial infections. Common nosocomial pathogens that primarily cause ventilator-associated pneumonia are gram-positive bacteria, such as methicillin-resistant *Staphylococcus aureus*, methicillin-resistant coagulase-negative *Staphylococci*, and *Enterococci* species. For the treatment of such infections, vancomycin 15 mg/kg IV over 8–12 hours, with or without a loading dose, was advised. Sub-optimal vancomycin doses were common; however because of the limited treatment window and individual differences, there was either insufficient antibacterial activity or a higher risk of acute renal injury. Thus, Therapeutic Drug Monitoring (TDM) of vancomycin is required to assure its clinical impact while reducing the likelihood of adverse effects. According to the guidelines, in order to maximize therapeutic effectiveness and reduce the risk of Acute Kidney Injury (AKI) in patients with severe MRSA infections, an AUC0-24/MIC ratio of 400 to 600 should be used in both adult and pediatric patients. Plasma or serum concentration can also be used as a substitute for AUCs since they are frequently unavailable in clinical practice. The Chinese Pharmacological Society's recommendations were for a serum trough level of 10–20 mg/L for severe MRSA infections and 10–15 mg/L for adult patients. Furthermore, it was predicted that the peak concentration would be lower than 40 mg/L.

The widespread hospitalization of COVID-19 patients, a significant fraction of who require mechanical ventilation, may lead to an increase in the use of vancomycin for the treatment of hospital-acquired infections, particularly Ventilator-Associated Pneumonia (VAP). Vancomycin pharmacokinetics in these patients, however, was not well understood. The choice of medicine dosage was based on clinical observations. As a result, in this investigation, we treated COVID-19 patients with vancomycin using ultra performance liquid chromatography/tandem mass spectrometry. The best doses were chosen based on the medication concentration. A prior study found that 15% of COVID-19-positive hospitalized patients also had secondary infections. The main pathogens in hospitalized (particularly ventilated) patients were 2 Gram positive bacteria. The fast rise in COVID-19-related hospitalization and ventilation underscored the importance of using vancomycin to treat gram-positive bacterial infections in these patients. TDM is essential for the rational use of vancomycin in order to keep the concentration at its ideal level and lower the risk of treatment failure, drug resistance, and kidney damage. Here, we discussed the preliminary results of TDM in COVID-19 patients. Hemodialysis, ECMO use, and renal impairment were the main things that had an impact on vancomycin's PK. Six of the eight subjects with COVID-19 had at least one of these variables at baseline, which suggests that these patients have difficulties justifying the use of vancomycin. Vancomycin serum concentrations were out of range in 25.4% (16/63) of the cases. 60% (3/5) of patients with baseline normal renal function experienced acute kidney damage after therapy. These emphasized the requirement of TDM for vancomycin treatment in COVID-19 patients. In samples taken before and after the start of TDM, abnormal concentration, particularly for peak spots, was more common (P= 0.05). It returned to and was sustained within the safe and effective range in three patients with aberrant trough and/or peak values after dose modification. In 7 of the patients (one is receiving emperical treatment), the target infection was clinically cured, and no vancomycin-associated nephrotoxicity was found during the TDM process. TDM might be a helpful technique to direct patients with COVID-19 in using vancomycin appropriately.

The COVID-19 patients frequently used hemodialysis, ECMO, and had functioning kidneys, emphasising the need for TDM. Vancomycin concentration was determined using a UPLC-MS/MS technique. Sixty-three blood samples were evaluated, and 16 of them exhibited concentrations that were higher than expected (10 at the lowest point and >40 mg/L at the highest

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point). In 37.5% of the patients, TDM-guided dose change produced the ideal concentration. No vancomycin-associated nephrotoxicity was found during the TDM process, and all patients were cured.