

Fecal Concentration of Intravenous Vancomycin Preparation in the Treatment of *Clostridioides difficile* Infection

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DESCRIPTION

In industrialised countries, *Clostridioides difficile* infection (CDI) is the leading cause of nosocomial diarrhoea. Its prevalence has recently increased in Europe and North America. There have been few studies in Latin America on the prevalence or incidence of CDI, so the true impact of the infection in our population is unknown. According to international guidelines for the treatment of CDI, oral antibiotics (metronidazole, vancomycin, and fidaxomicin) as well as other treatment modalities, such as faecal microbiota transplantation, are recommended. For many years, metronidazole was recommended as first-line treatment. However, due to CDI recurrence after metronidazole treatment, international guidelines have recommended oral vancomycin and Fidaxomicin as first-line drugs. The recommended vancomycin oral dosage is 125 mg to 500 mg QID for 10-14 days. However, the optimum CDI dose is unknown, whereas the minimum inhibitory concentration (MIC) is 0.5-8 mg/L and the minimum bactericidal concentration (MBC90) is greater than 1,000 mg/L.

According to the World Health Organization, antimicrobial resistance is one of the most serious global health threats of our time. As a result, efforts to optimize the use of antimicrobial medicines and develop sustainable innovation are among the goals of global actions. In low and middle-income countries, such as those in Latin America, insufficient access to antibiotics may coexist with excessive consumption, making distribution and regulation difficult. As a result, it is critical to provide scientific evidence on the proper use of those drugs at all levels. One example is the oral administration of vancomycin (either by off-label use of the parenteral presentation or by specific oral formulations), as its use in the treatment and prevention of active *Clostridioides difficile* Infection has increased (CDI). Although metronidazole is typically used in severe forms of CDI. Vancomycin usually outperforms it, especially in mild to moderate

diseases. The rationale for this substitution is that nearly 25% of patients experience disease recurrence after initial treatment, with 35% experiencing a second recurrence. Furthermore, metronidazole resistance has been reported in CDI ranging from 0% to 18.3% and can be unstable, inducible, and heterogeneous. Furthermore, vancomycin has good water solubility, protease stability, and no metabolism, and its poor gastrointestinal absorption results in high intracolonic drug levels. When CDI is confined to the colon, long-term therapy is required, and systemic adverse events may complicate baseline health conditions, this is clearly an advantage. A low-dose regimen of intravenous vancomycin (125 mg every 6 hours) demonstrated no detectable drug in the serum of patients with varying levels of renal function. According to other reports, higher doses (500 mg vancomycin capsules), severe CDI (with increased intestinal permeability), and renal compromise (supportive dialysis) are risk factors for systemic vancomycin absorption following oral administration. Because of the effects of assay detection limits, associated morbidities, concomitant drugs, and dosage regimens, the findings on the non-absorbable property of oral vancomycin administration are inconclusive. Nonetheless, when compared to the known systemic effects of intravenous vancomycin, the risk-benefit balance is favorable (ototoxicity, nephrotoxicity).

It is important to remember that the most feared adverse event for vancomycin, "red man syndrome," has been reported with both intravenous and oral administration, and is unrelated to systemic drug concentration. Several important messages can be highlighted: first, that stool concentration is dose-dependent (mouse dosing equivalent to 125 mg and 500 mg in humans); second, that vancomycin showed significant concentration as soon as 2 h post dose; and third, that at 6 h, the low-dose regimen showed a decrease in vancomycin stool concentration (below the 2 h data), confirming the need for a 6 h administration schedule.

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