Comparative Efficacy and Safety of Vancomycin Dosage Adjustment by Equation-based Method versus Trough Concentration Method for Treatment of Infections Caused by Methicillin Resistant *Staphylococcus Aureus*: Preliminary Results of Randomized Controlled Trial

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**Background:** Vancomycin is widely used for treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections. The 24-hour area under the curve/minimum inhibitory concentration (AUC24/MIC) of ≥400 is associated with good clinical response in MRSA treatment. Given that calculation of the AUC24/MIC is not practical because it requires multiple points of serum vancomycin level measurement, maintaining a single-point trough vancomycin level of 15-20 mg/L can be widely acceptable for treatment of serious MRSA infections. However, the Equation-based method that requires only two points of serum vancomycin level measurement has been proved to be strongly correlated with the AUC24/MIC. Therefore, the equation-base method may be used for vancomycin dosage adjustment.

**Objective:** To compare the efficacy and safety of different methods of vancomycin dosage adjustment for treatment of MRSA infections.

**Materials:** A single center, randomized controlled trial was conducted at Siriraj Hospital. We enrolled hospitalized patients with MRSA infections who required parenteral vancomycin for ≥3 days. The patients were randomly assigned to receive the vancomycin dosage adjustment by either the equation-based method (intervention) or the trough concentration method (control). The outcomes of interest included clinical cure rate, 28-day mortality, and renal adverse events.

**Results:** During a study period (October 2016 – December 2017), we enrolled 4 patients into the intervention group and 6 patients into the control group. The most common site of infection was bacteremia (75.0%) in the intervention group and pneumonia (50.0%) in the control group. (P=0.47). There was no significant difference in the favorable clinical response (intervention vs control) on the day-7 (75.0% vs 83.3%; P=0.67) and at the end of therapy (100.0% vs 83.3%; P=1.00). No significant difference in the 28-day mortality was detected (25.0% vs 16.7%; P=1.00). One case in the intervention group (25.0%) and none in the control group experienced doubling serum creatinine at the end of therapy (P=0.40). Probability to achieve the target vancomycin parameter at the 96-hr time point was slightly higher in the intervention group (50% vs 33.3%; P=0.20) as well as at the 120-hr time point (100.0% vs 50.0%; P=0.20).

**Conclusion:** Although our preliminary study could not demonstrate the superiority of the equation-based method in term of all treatment outcomes, patients in the intervention group seem to be more likely to achieve the target vancomycin parameter than those in the control group. However, the larger sample size is suggested to confirm the efficacy and safety of vancomycin dosage adjustment by equation-based method.

**Keywords:** MRSA, Vancomycin, Equation, Trough level