Model-Based Sotalol Pediatric Dosing Recommendations

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Objectives: Sotalol is approved in pediatrics to treat atrial and ventricular arrhythmia. The label dosing recommendations based on body surface area (BSA) and age-dependent renal maturation are prone to error calculations due to their complexity. Patients under sotalol need to be monitored for QTc prolongation for at least 3 days until steady-state exposure is reached. Our objectives are, first, to provide a dosing chart based on body weight (BW) and age, secondly, to develop an IV/Oral switch regimen to reduce length of hospital stay.

Methods: Parameters from a sotalol population pharmacokinetic model¹ was used to develop an easy to use BW based dosing chart as opposed to BSA. Three different BW-only based formulae (Livingston and Lee, Boyd and Costeff) were evaluated as an alternative to Mosteller formula to estimate BSA. Model-based simulations were performed to determine an optimal IV loading dose before switching to an oral maintenance regimen.

Results: Costeff formula provided the closest estimation to the BSA-based doses with a median bias (95% CI) of 0% (-3.6% to 2.8%) and 0.6% (-3.1% to 5.7%) for the 0-2 years and 2-20 years old age groups, respectively. The resulting dosing charts for treatment initiation are illustrated in Figure 1. An IV loading dose of 1.5 mg/kg over a 2-hour infusion followed by the recommended t.i.d oral sotalol initiation dose is the optimal dosing regimen that would allow the achievement of target exposures in neonates. For patients older than 1 month, an IV loading dose corresponding to half of the recommended oral dose infused over 1 hour, followed by the regular oral dosing regimen allowed to achieve the target exposure on day 1.

Conclusions: The proposed dosing chart based on age and BW, provides clinicians with a useful tool for dose selection, consistent to the label-approved doses. We also provide a safe alternative to use IV sotalol formulation in clinics to optimize sotalol therapy and to facilitate early attainment of target exposures.

References:

Figure 1. Sotalol dosing nomogram, equivalent to the approved 30 mg/m^2 t.i.d, in patients with normal renal function: (upper panel) neonates and infants from 0 to 2 years old and (Lower panel) children and adolescent from 2 to 17 years old.