

Safety and Effect on Length of Stay of Intravenous Sotalol Initiation for Arrhythmia Management

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Sotalol is a class III antiarrhythmic drug with beta-adrenergic blocking activity, used to manage both supraventricular and ventricular arrhythmias. It is available in both oral and intravenous formulations^[1]. The FDA approved intravenous Sotalol in March 2020. Sotalol is known to cause QTc prolongation with serum sotalol concentration linearly correlating with QTc length regardless of the route of administration^[2,3], with women being at higher risk than men^[4]. QTc interval prolongation is one of many parameters that is associated with cardiovascular mortality^[5]. QTc prolongation may lead to polymorphic ventricular tachycardia/Torsade de Pointes which is a potentially lethal condition that is acquired from medications or

due to an underlying channelopathy predisposing to sudden cardiac arrest^[6]. Additional adverse effects of sotalol may include hypotension, bradycardia and AV block^[7,8]. Nevertheless, since its approval, IV sotalol has been successfully and safely used in both adult and pediatric patient populations for the management of arrhythmias in acute and chronic settings ^[9,10,11,12]. Initiation of sotalol therapy with PO loading requires 5 successive oral doses over a 3-day hospital stay for monitoring, at an estimated cost of \$2931.55 per day ^[13]. In 2020, a protocol for IV loading of sotalol was developed using data modeling. This protocol was hypothesized to allow a significant reduction in the length of hospitalization, and thus in the incurred costs^[14]. However, there has not been any large-scale implementation of this protocol, nor any comparison of its safety profile and efficacy to that of the traditional oral loading protocol.

This study by Liu et al. is a nonrandomized clinical trial in which 29 patients underwent IV sotalol loading. They were compared by chart review to 20 patients who underwent PO sotalol loading in the same timeframe. The indication for sotalol initiation in both cases was for primary atrial or ventricular arrhythmias. The study's main aim was to assess the safety profile of IV sotalol loading while comparing the length of hospitalization to that required for PO sotalol loading. The same exclusion and inclusion criteria were applied to both groups. Notably, patients with significantly depressed LVEF and creatinine clearance were excluded. The study revealed that safety outcomes were similar in both groups but that IV sotalol loading led to significantly shorter hospital stays. It also found that QT or QTc in patients receiving IV sotalol was similar at the conclusion of the one-hour infusion to that at discharge.

These findings support the use of IV loading for sotalol initiation, as they suggest it requires shorter hospital stays than PO loading with similar safety profiles. As shorter hospital stays translate into lower patient days, lower costs, and these results suggest IV sotalol loading is more cost-efficient than its oral counterpart. They also suggest that the maximal increase in QT or QTc length following sotalol initiation is attained by the end of IV loading, thus indicating that patients may be discharged within less than 24 hours of drug initiation.

While this study offered valuable insight, its design had significant limitations. Firstly, this was not a randomized clinical trial. A comparison of baseline characteristics between the two populations studied revealed a significantly higher proportion of females in the oral group, which may have inherently skewed outcomes related to QT and QTc length.

Secondly, the sample size was small, with no long-term follow-up. Lastly, patients with significantly depressed GFR or LVEF, particularly prone to developing adverse effects with sotalol use, were excluded from the study. Randomized clinical trials examining the short-term and long-term safety of IV sotalol loading and the optimal length of hospitalization are needed, and such efforts are already underway.

References:

1. Batul, S. A., & Gopinathannair, R. (2017). Intravenous Sotalol - Reintroducing a Forgotten Agent to the Electrophysiology Therapeutic Arsenal. *Journal of atrial fibrillation* , 9 (5), 1499. <https://doi.org/10.4022/jafib.1499>
2. Somberg, J. C., Preston, R. A., Ranade, V., & Molnar, J. (2010). QT prolongation and serum sotalol concentration are highly correlated following intravenous and oral sotalol. *Cardiology* , 116 (3), 219–225. <https://doi.org/10.1159/000316050>
3. Barbey, J. T., Sale, M. E., Woosley, R. L., Shi, J., Melikian, A. P., & Hinderling, P. H. (1999). Pharmacokinetic, pharmacodynamic, and safety evaluation of an accelerated dose titration regimen of sotalol in healthy middle-aged subjects. *Clinical pharmacology and therapeutics* , 66 (1), 91–99. [https://doi.org/10.1016/S0009-9236\(99\)70058-5](https://doi.org/10.1016/S0009-9236(99)70058-5)
4. Somberg, J. C., Preston, R. A., Ranade, V., Cvetanovic, I., & Molnar, J. (2012). Gender differences in cardiac repolarization following intravenous sotalol administration. *Journal of cardiovascular pharmacology and therapeutics* , 17 (1), 86–92. <https://doi.org/10.1177/1074248411406505>
5. Al-Kindi SG, Refaat M, Jayyousi A, Asaad N, Al Suwaidi J, Abi Khalil C. Red Cell Distribution Width is Associated with All-Cause and Cardiovascular Mortality in Patients with Diabetes. *Biomed Res Int*

2017; 2017: 5843702

6. Refaat MM, Hotait M, Tseng ZH: Utility of the Exercise Electrocardiogram Testing in Sudden Cardiac Death Risk Stratification. *Ann Noninvasive Electrocardiol* 2014; 19(4): 311-318.
7. Marill, K. A., & Runge, T. (2001). Meta-analysis of the Risk of Torsades de Pointes in patients treated with intravenous racemic sotalol. *Academic emergency medicine*, 8 (2), 117-124. <https://doi.org/10.1111/j.1553-2712.2001.tb01275.x>
8. MacNeil, D. J., Davies, R. O., & Deitchman, D. (1993). Clinical safety profile of sotalol in the treatment of arrhythmias. *The American journal of cardiology*, 72 (4), 44A-50A. [https://doi.org/10.1016/0002-9149\(93\)90024-7](https://doi.org/10.1016/0002-9149(93)90024-7)
9. Malloy-Walton, L. E., Von Bergen, N. H., Balaji, S., Fischbach, P. S., Garnreiter, J. M., Asaki, S. Y., Moak, J. P., Ochoa, L. A., Chang, P. M., Nguyen, H. H., Patel, A. R., Kirk, C., Sherman, A. K., Avari Silva, J. N., & Saul, J. P. (2022). IV Sotalol Use in Pediatric and Congenital Heart Patients: A Multicenter Registry Study. *Journal of the American Heart Association*, 11 (9), e024375. <https://doi.org/10.1161/JAHA.121.024375>
10. Borquez, A. A., Aljohani, O. A., Williams, M. R., & Perry, J. C. (2020). Intravenous Sotalol in the Young: Safe and Effective Treatment With Standardized Protocols. *JACC. Clinical electrophysiology*, 6 (4), 425-432. <https://doi.org/10.1016/j.jacep.2019.11.019>
11. Kerin, N. Z., & Jacob, S. (2011). The efficacy of sotalol in preventing postoperative atrial fibrillation: a meta-analysis. *The American journal of medicine*, 124 (9), 875.e1-875.e8759. <https://doi.org/10.1016/j.amjmed.2011.04.025>
12. Milan, D. J., Saul, J. P., Somberg, J. C., & Molnar, J. (2017). Efficacy of Intravenous and Oral Sotalol in Pharmacologic Conversion of Atrial Fibrillation: A Systematic Review and Meta-Analysis. *Cardiology*, 136 (1), 52-60. <https://doi.org/10.1159/000447237>
13. Varela, D. L., Burnham, T. S., T May, H., L Bair, T., Steinberg, B. A., B Muhlestein, J., L Anderson, J., U Knowlton, K., & Jared Bunch, T. (2022). Economics and outcomes of sotalol in-patient dosing approaches in patients with atrial fibrillation. *Journal of cardiovascular electrophysiology*, 33 (3), 333-342. <https://doi.org/10.1111/jce.15342>
14. Somberg, J. C., Vinks, A. A., Dong, M., & Molnar, J. (2020). Model-Informed Development of Sotalol Loading and Dose Escalation Employing an Intravenous Infusion. *Cardiology research*, 11 (5), 294-304. <https://doi.org/10.14740/cr1143>