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Dominance of Furosemide for Loop Diuretic Therapy in Heart Failure:

Time to Revisit the Alternatives?

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To the Editor

Diuretics are a mainstay of treatment in both chronic and acute decompensated heart failure (HF). Studies during the 1990s and early 2000s show that roughly 90% of HF patients receive at least 1 class of diuretics, particularly a loop diuretic, for management of chronic (1,2) or acute (3) HF. There are at least 3 widely known loop diuretics—furosemide, bumetanide, and torsemide—all of which are available as generic formulations.

The available evidence suggests that newer loop diuretics and furosemide may not be identical. Although markedly limited by methodological problems and inadequate power, the few existing pharmacological and clinical studies propose that there might be superior and more consistent oral bioavailability, longer duration of action, improved tolerability, and better outcomes with newer loop diuretics, particularly torsemide, as compared with

furosemide (4–7). Unlike bumetanide for which there is a dearth of clinical studies, only a few small studies have compared the effects of torsemide versus furosemide. The TORIC (Torasemide In Congestive Heart Failure) study, an open-label study of 1,337 patients with New York Heart Association class II to III HF, was the largest study comparing furosemide with newer loop diuretics. Although the study had several methodological limitations, TORIC showed that a greater proportion of patients receiving torsemide improved their functional class (45.8% vs. 37.2%, $p < 0.00017$) and that fewer patients receiving torsemide died (2.2% vs. 4.5%, $p < 0.05$) (5). Additionally, a meta-analysis of the existing studies (4–6,8–10) (Fig. 1), although demonstrating remarkable heterogeneity, suggests trends toward improved functional status and mortality with torsemide compared with furosemide. Previous research also suggested that torsemide could be cost-saving compared with furosemide (11). Although there are no existing clinical studies that have compared the efficacy of newer loop diuretics versus furosemide for episodes of acute HF, it might be possible that the newer agents are also beneficial in various stages of care of acutely decompensated HF. In light of the potential advantages of newer loop diuretics, we sought to characterize current patterns of use of these agents in U.S. hospitals.

Using the data from the Perspective database, a voluntary, fee-supported database of more than 500 U.S. hospitals developed by Premier, Inc., we studied HF hospitalizations during 2009 and 2010 to determine the proportion of adult (age >18 years) patients treated with major loop diuretic formulations. We identified HF hospitalizations by the International Classification of Diseases-Ninth Revision-Clinical Modification principal discharge codes: 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, or 428.xx.

Among the 274,515 patients with a principal discharge diagnosis of HF in the Perspective database, 251,472 (92%) patients received loop diuretic therapy during their hospital stay. Of those, 218,787 (87%) received furosemide as their only loop diuretic, 6,776 (3%) only received bumetanide, 972 (0.4%) only received torsemide, whereas 24,937 (10%) were treated with a combination of these agents.

Most patients with HF received a loop diuretic. However, torsemide, a new agent with potentially superior clinical effectiveness, was rarely used. Given the common usage of loop diuretics in HF and their potential nonequivalence in HF outcomes and safety endpoints, perhaps it is time for well-designed randomized controlled trials, powered for clinical endpoints such as mortality, readmission, and quality of life, to determine whether there are differences in the safety and effectiveness of these agents both for management of chronic HF and for episodes of acute decompensation.

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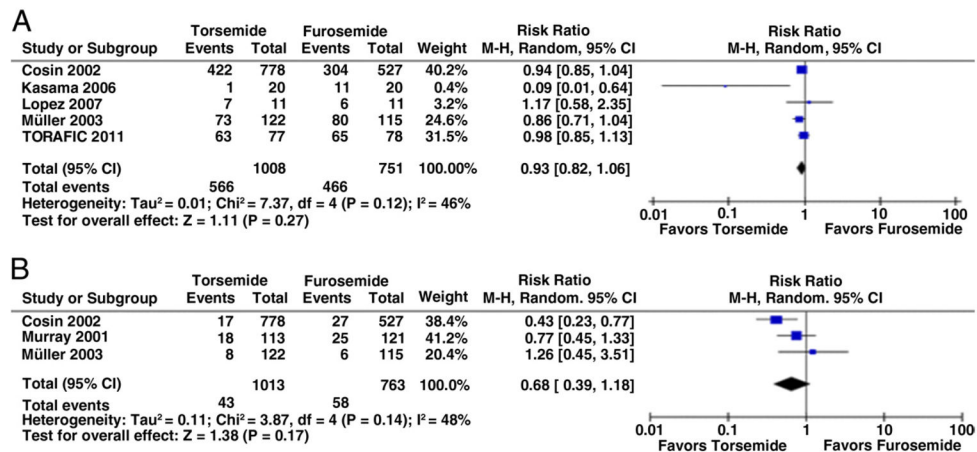


Figure 1. Functional Status and Mortality With Torsemide Compared With Furosemide
 No improvement in New York Heart Association functional classification (**A**) and all-cause death (**B**) with torsemide versus furosemide. CI = confidence interval; M-H = Mantel-Haenszel.