Published Online, 20 October 2009, www.theannals.com, DOI 10.1345/aph.1M177.
The Annals of Pharmacotherapy: Vol. 43, No. 11, pp. 1836-1847. DOI 10.1345/aph.1M177

INTERNAL MEDICINE

A Comprehensive Review of the Loop Diuretics: Should Furosemide Be First Line?

Kurt A Wargo, PharmD BCPS

Associate Clinical Professor, Division of Internal Medicine, Auburn University Harrison School of Pharmacy, University of Alabama at Birmingham Huntsville Regional Medical Campus, Huntsville, AL

William M Banta, PharmD

at time of writing, Pharmacy Student, Auburn University Harrison School of Pharmacy

Reprints: Dr. Wargo, Auburn University Harrison School of Pharmacy, 301 Governors Dr. SW, Suite 385 C1, Huntsville, AL 35801, fax 256/551-4567, wargoka@auburn.edu

OBJECTIVE: To review the literature regarding the pharmacokinetic profiles, comparative safety and efficacy, and comparative costs of loop diuretics to evaluate the current clinical usefulness of furosemide.

DATA SOURCES: A search of MEDLINE (1966–June 2009) was conducted using the terms furosemide, torsemide, bumetanide, ethacrynic acid, and loop diuretics. Articles were limited to those written in English.

STUDY SELECTION AND DATA EXTRACTION: All English-language articles identified from the data sources were reviewed. Studies were eligible if they encompassed pharmacokinetics, comparative safety and efficacy, or comparative costs of the loop diuretics.

DATA SYNTHESIS: In patients with heart failure (HF), torsemide demonstrated decreased mortality compared with furosemide in 1 study (2.2% vs 4.5% in the furosemide group; $p < 0.05$), decreased hospitalizations in 1 study (23 in the torsemide group vs 61 in the furosemide group; $p < 0.01$), and improved New York Heart Association functional classifications in 2 studies. In the first, 45.8% with torsemide versus 37.2% with furosemide demonstrated improvement in at least one functional class ($p = 0.00017$). In the second, 40.2% with torsemide and 30.7% with furosemide demonstrated improvement in at least one functional class ($p = 0.014$). In 2 of 3 studies of patients with cirrhosis, torsemide increased natriuresis and total volume diuresed compared with furosemide in patients with cirrhosis; however, no significant difference between the agents with respect to plasma renin and aldosterone concentrations was demonstrated. In patients with pulmonary hypertension, central venous pressure, capillary wedge pressure, and stroke volume significantly improved from baseline among patients who received torsemide, but not in those who received furosemide, although the intergroup analysis failed to reach statistical significance. Among patients with chronic kidney disease, no significant differences were noted with respect

to natriuresis and blood pressure control between the 2 agents; however, in patients with acute kidney injury, patients who received furosemide had a significant improvement in urine output versus the torsemide group. Additionally, 2 trials comparing bumetanide with furosemide were identified, although the results were conflicting. In patients with nephrotic syndrome, bumetanide significantly improved weight loss in the first 4 weeks and in week 20, compared with furosemide. In patients with HF, significant improvement in dyspnea at rest and on exertion was exhibited in the bumetanide group, but not in the furosemide group; no significant difference was noted between the 2 groups when evaluating global assessment.

CONCLUSIONS: Growing evidence demonstrates more favorable pharmacokinetic profiles of torsemide and bumetanide compared with furosemide. Furthermore, torsemide may be more efficacious and safer than furosemide in patients with HF. A trial comparing all 3 drugs would be required to confirm torsemide as the primary loop diuretic in patients with HF, but based upon limited current evidence, we recommend torsemide over furosemide. Currently, little evidence exists to support either torsemide or bumetanide as first-line treatment over furosemide in patients with other edematous disease states.

Key Words: bumetanide, ethacrynic acid, furosemide, loop diuretics, torsemide

Published Online, October 20, 2009. *www.theannals.com*, DOI 10.1345/aph.1M177

THIS ARTICLE IS APPROVED FOR CONTINUING EDUCATION CREDIT
ACPE UNIVERSAL PROGRAM NUMBER: 407-000-09-019-H01-P