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Effect of torsemide and furosemide on clinical, laboratory, radiographic and quality of life variables in dogs with heart failure secondary to mitral valve disease

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Abstract *Objectives:* Diuretic therapy reduces preload and relieves congestion secondary to cardiac dysfunction. Torsemide (torasemide) is a loop diuretic with longer duration of action, decreased susceptibility to diuretic resistance, and adjunctive aldosterone antagonist properties compared with furosemide. We hypothesized that torsemide would be well tolerated and no less effective than furosemide at diuresis, control of clinical signs, and maintenance of quality of life (QOL) in dogs with congestive heart failure (CHF).
Animals, materials and methods: Seven client-owned dogs with stable CHF receiving twice daily oral furosemide and adjunctive medications. Utilizing a double-blinded, randomized, crossover design, dogs were administered either oral furosemide at their current dose or an equivalent oral dose of torsemide (1/10 of the daily furosemide dose divided into twice daily dosing) on day 0. Crossover occurred at day 7 and the study ended on day 14. Clinical, laboratory, radiographic, and QOL variables were evaluated on days 0, 7 and 14.
Results: No dogs developed recurrent CHF during the study. Mean furosemide dose on day 0 was 5.13 mg/kg/day (range 2.8—9.6). Following torsemide treatment, creatinine ($P = 0.020$), urea nitrogen ($P = 0.013$), phosphorus ($P = 0.032$), albumin

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($P = 0.019$), carbon dioxide ($P = 0.015$) and anion gap ($P = 0.005$) were significantly increased, and urine specific gravity ($P = 0.004$) and chloride ($P = 0.021$) were significantly decreased compared with furosemide dosing. No differences in QOL were found.
Conclusions: Results indicate that torsemide is equivalent to furosemide at controlling clinical signs of CHF in dogs and is likely to achieve greater diuresis vs. furosemide. Larger clinical trials evaluating torsemide as a first or second-line loop diuretic for congestive heart failure in dogs are warranted.

Abbreviations

ACEI	angiotensin-converting enzyme inhibitors
BUN	blood urea nitrogen
CHF	congestive heart failure
FETCH	Functional Evaluation of Cardiac Health
QOL	quality of life
USG	urine specific gravity

Introduction

Loop diuretics are a mainstay of treatment for CHF in human and veterinary patients because of their ability to reduce intravascular hydrostatic pressure and reduce the clinical signs associated with edema formation.[1,2] Furosemide[b] and torsemide[c] (torasemide) are loop diuretics commonly used in humans.[3] While furosemide is commonly used in veterinary patients with CHF, the use of torsemide in veterinary medicine is not well described. Torsemide (1-isopropyl-3[(4-m-toluidino-3-pyridyl) sulphonyl]urea) is a pyridyl sulfonylurea with a chemical structure between that of traditional loop diuretics and Cl- channel blockers.[4,5] Its primary site of action is the thick ascending loop of Henle in the nephron, where it promotes excretion of sodium, water, and chloride via interaction with the Na^+, K^+, $2Cl^-$ cotransporter.[4,6,7] In humans, torsemide has a higher bioavailability, longer half-life, and longer duration of action than furosemide, resulting in a more uniform action of diuresis that is both stronger and more effective.[8,9]

Torsemide's safety and efficacy are well established in human patients with CHF. A recent review cited evidence that torsemide has more favorable pharmacokinetics, efficacy, and safety than furosemide in patients with heart failure and recommended that torsemide be considered a first-line therapy in humans with heart failure.[10] The TORIC study (Torasemide in Congestive Heart Failure) demonstrated a significantly lower total mortality/cardiac mortality, greater improvement in New York Heart Association (NYHA) functional heart failure class and reduction in hospital readmission rate in human patients treated with torsemide (compared with furosemide and other diuretics).[9] These findings have been duplicated in subsequent studies.[3,8] Torsemide's superiority over furosemide is likely due to antifibrotic effects on the myocardium as well as blunting of loop diuretic resistance, effects that appear mediated by torsemide's antagonism of aldosterone in a manner similar to that of spironolactone[d].[11,12] Addition of spironolactone to treatment regimens in human CHF patients significantly reduces mortality and a recent study in dogs supports improved survival in dogs with ISACHC class II and III degenerative mitral valve disease with spironolactone therapy.[13,14] Torsemide also improves cardiac sympathetic nerve activity and decreases plasma brain natriuretic peptide (BNP) levels in humans with CHF. These parameters have been demonstrated to be strong prognostic indicators for survival in humans with CHF.[15]

Limited data exists on the use of torsemide as a diuretic or in treatment of CHF in dogs and its effects on laboratory parameters and clinical signs have not been directly compared with furosemide. A small study in a group of dogs with CHF secondary to degenerative mitral valve disease evaluated serum and urine electrolytes during short-term use of

[b] Lasix, Sanofi-Aventis U.S. LLC, Bridgewater, NJ.
[c] Demadex, Meda Pharmaceuticals Inc., Somerset, NJ.
[d] Aldactone, Pfizer Inc, New York, NY.