Comparison between Furosemide and Torsemide in Patients with Acute Decompensated Heart Failure, which is better

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Abstract

Objectives: assess the benefit of shifting from furosemide to torsemide versus adjusting furosemide dose on heart failure hospitalisation within six months of discharge following acute decompensated heart failure.

Study design: This study was performed in the National Heart Institute in Egypt, and it had two phases; *phase 1* compared the time to hospitalization for heart failure within one month and 6 months from discharge for patients already on furosemide and were shifted to torsemide and patients who received higher dose of furosemide upon discharge. *Phase 2* analysed the clinical characteristics of the two groups to determine switching predictors of furosemide into torsemide. All patients with decreased or maintained LVEF% were categorized into two groups; *Group 1* included patients who were on furosemide and discharged on a higher dose of furosemide than the dose before admission. *Group 2* included all patients who were on furosemide and discharged on torsemide.

Results: the mean age of included patients was 67 ±11.7 years, 54.3% were males. Within one month following discharge, torsemide usage resulted in decrease in HF hospitalisation (P-value=0.57), and hospitalisation for HF within six months of discharge did not vary significantly between two groups (P-value=0.87). aldosterone antagonist utilization increased the likelihood of prescribing torsemide. On the other hand, ACE inhibitors, ARBs, and age were negative predictors of torsemide usage.

Conclusions: Shifting furosemide to an equivalent furosemide dose following acute decompensated heart failure did not result in a reduction in HF hospitalisation when compared to dose optimization of furosemide.

Keywords: *diurtics, heart failure, hospital mortality, morbidity*,

Abbreviations, acronyms& symbols	
HF	Heart Failure
LVEF%	Left Ventricular Ejection Fraction%
IHD	Ischemic Heart Disease
ACE(-)	Angiotensin-Converting Enzyme inhibitors
ARBs	Angiotensin 2 Receptor Blockers
AF	Atrial Fibrillation
VHD	Valvular Heart Disease

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Introduction

Heart failure (HF) is a leading cause of mortality and hospital admission. The new HF guidelines suggest loop diuretics use, such as furosemide and torsemide, to treat volume overload and alleviate symptoms in individuals with acute and chronic HF [(1-2)].

Although torsemide has longer half-life and higher bioavailability than furosemide (about 50% in furosemide vs >80% in torsemide) [(3)], furosemide remains the most commonly used loop diuretic in patients with heart failure.

Acute decompensated heart failure patients who were previously receiving oral furosemide should get an intravenous dose equivalent to or more than the oral dose to minimize volume overload [(1-2)].

Upon discharge and when volume overload had been relieved, these patients may continue on a higher dose of furosemide than their previous dose before admission to avoid volume overload recurrence [(1)].

Beside the advantage of torsemide over furosemide in its higher bioavailability and longer half-life, torsemide has a beneficial effect on the neurohormonal axis and a protective effect on the ventricular structure[(4)], which increases its usage in decompensated heart failure patients who were previously treated with furosemide or another diuretic before admission[(5)].

Data guiding diuretic dose after decompensated heart failure and the subsequent outcome are limited.

Numerous clinical trials comparing torsemide to furosemide in heart failure indicated that torsemide had a lower risk of mortality and morbidity; however, these trials included chronic heart failure patients who were hospitalized for decompensated heart failure and did not assess shifting from furosemide to torsemide for optimising furosemide doses on discharge[(6–7)].

This study aimed to determine the value of shifting from furosemide to torsemide compared to increasing the dose of furosemide on discharge in acute decompensated heart failure patients on admission and to determine the predictors of shifting from furosemide to torsemide upon discharge.

Aim of the work

To evaluate the effect of shifting furosemide to torsemide versus adjusting furosemide dose on heart failure hospitalisation after one and six months of discharge following acute decompensated heart failure.

Methods

This study was performed in the National Heart Institute in Egypt, and it had two phases; phase 1 compared the time to hospitalization for heart failure within one month and 6 months from discharge for patients already on furosemide and were shifted to torsemide and patients who received higher dose of furosemide upon discharge. Phase 2 analysed the clinical characteristics of the two groups to determine switching predictors of furosemide into torsemide.

This study included all patients with decreased or maintained LVEF% who were hospitalised for acute decompensated HF and were on furosemide prior to admission.

Patients were categorized into two groups; **Group 1** included patients who were on furosemide and discharged on a higher dose of furosemide than the dose before admission. **Group 2** included all patients who were on furosemide and discharged on torsemide.

The outcome was measured for

1. Time to first readmission because of acute decompensated heart failure within 1 and 6 months of discharge for group 1 and group 2.
2. The factors that influence the decision to switch from furosemide to torsemide in patients having heart failure who were taking furosemide prior to hospitalisation for acute decompensated heart failure.

Adjustments were made for clinically significant variables associated with HF decompensation,such as age, sex, LVEF%, weight, serum sodium and potassium, serum creatinine,

valvular heart disease, IHD, and drugs such as ACE, ARBs, beta-blockers, lanoxin, and aldosterone antagonists.

Upon discharge, total daily diuretic doses were calculated on the basis of converted torsemide to furosemide equivalents as 20 mg torsemide equivalents to 40 mg furosemide [2 – 3].

Statistical analysis

The SPSS software was used to perform the statistical analysis. For categorical variables, frequencies with percentages were used,and means with standard deviation were provided for numerical variables. The chi-square test was used for comparing categorical variables, while the Student's t-test was utilized to compare numerical variablesbetweenthe two groups.

Cox proportional hazard regression analysis was used to assess the relation between torsemide utilization and duration of hospitalisation at 30 days and 6 months after discharge.

The predictors of shifting furosemide to torsemide in heart failure patients were determined using multivariate logistic regression.

Results

This study involved 464 individuals with acute decompensated HF. They were all on furosemide prior to admission. Of these patients, 374 patients were discharged on an optimal furosemide doses, while 90 patients were discharged on torsemide.

Table 1 shows that the mean age was 67 ±11.7 years. About half of the patients (54.3%) were males, and 45.7% were females. More than half of the patients (56.9%) had an ejection fraction of less than 40%, and 43.1% had an ejection fraction greater than 40%. Most patients in group 1 were found to have ischemic heart disease, where as most patients in group 2 were found to have a greater prevalence of valvular heart disease.

The furosemide baseline total daily dose was significantly higher in group 2 than in group 1, and the total daily dose of diuretic at discharge expressed in furosemide equivalents was not statistically significant between two groups. Thus,from hospitalisation to discharge, diuretic dose mean change was significantly lower in group 2 than in group 1.

Table 1:Baseline characteristics of the patients included in the study

Item	Total	Group 2	Group 1	P-value
Sex	252 males (54.3%), 212 (45.7%) females	48 males (53.3%) and 42 (46.7%) females	204 males (54.5%) and 170 (45.5%) females	0.88
Age*	67 +/- 11.7	65+/- 10.7	67+/-11.9	0.23
Weight	83+/-23.9	88+/-24.3	82+/-23.7	0.15
LVEF% <40%	264 (56.9%)	44 (48.8%)	220 (58.8%)	
LVEF% >40%	200 (43.1%)	46 (51.1%)	154 (41.1%)	
Heart rate*	74+/-12.8	74+/-12.6	74+/-12.9	0.87
hypertension	398 (85.8%)	78 (86.7%)	320 (85.6%)	0.85
Diabetes	370 (79.7%)	68 (75.6%)	302 (80.7%)	0.44
dyslipidaemia	114 (24.6%)	18 (20.0%)	96 (25.7%)	0.43
Serum creatinine*	1.55+/-0.9	1.62+/-0.72	1.52+/-0.98	0.51
Serum K^{+*}	4.2+/-0.46	4.15+/-0.4	4.19+/-0.47	0.55
Serum Na^{++*}	137+/-4.4	137+/-4.8	137+/-4.3	0.82
Baseline furosemide (mg)*	66+/-39	101+/-47	57+/-31	<0.001
Intravenous furosemide	444 (95.7%)	80 (88.9%)	364 (97.3%)	0.026
Atrial fibrillation	140 (30.2%)	34 (37.8%)	106 (28.3%)	0.22
IHD	316 (68.1%)	48 (53.3%)	268 (71.7%)	0.018
VHD	97	25	72	0.23
Renal impairment	198 (42.7%)	44 (48.9%)	154 (41.2%)	0.35
Diabetes	370 (79.7%)	68(75.6%)	302(80.7%)	0.44
Hypertension	398(85.8%)	78(86.7%)	320(85.6%)	0.85
Dyslipidemia	114(24.6%)	18(20.0%)	96(25.7%)	0.43

Values are expressed as mean +/-SD.

Table 2: Concurrent drugs

Drug	Total patients	Group 2	Group 1	P-value
ACE ihibitors	162 (34.9%)	24 (26.6%)	138 ((36.9%)	0.2
ARBs	112 (24.1%)	16 (17.8%)	96 (25.7%)	0.27
Thiazide like diuretics	40 (8.6%)	14 (15.6%)	26 ((7.0%)	0.08
Beta blockers	414 (89.2%)	74 (82.2%)	340 (90.9%)	0.11
Aldosterone antagonists	168 (36.2%)	40 (44.4%)	128 (34.2%)	0.2
Calcium channel blockers	142 (30.6%)	22 (24.4%)	120 (32.1%)	0.34
Ivabradine	12 (2.6%)	0 (0.0%)	12 (3,2%)	0.6
Lanoxin	56 (12.1%)	8 (8.9%)	48 (12.8%)	0.47
Sacubitril/valsartan	8 (1.7%)	2 (2.2%)	6 (1.6%)	0.58
Total daily dose of diuretic	216 +/-48	192 +/-54	220 +/-46	0.07
Nitrates	204 ((44.0%)	36 (40%)	168 (44.9%)	0.55

ACE Angiotensin-converting enzyme
ARBs Angiotensin 2 receptors blockers

Table 2 shows that the number of patients in group 2 who were on thiazide-like diuretic was twice the number in group 1, and more patients were on aldosterone antagonists than in group 1. On the other hand, more patients in group1 used ACE inhibitors, beta-blockers and lanoxin.

Within one month following discharge, torsemide usage resulted in decrease in HF hospitalisation, but after adjustment for the variables associated with HF hospitalisation, the HF within 30 days did not change significantly between the two groups, as shown in **figure 1**.

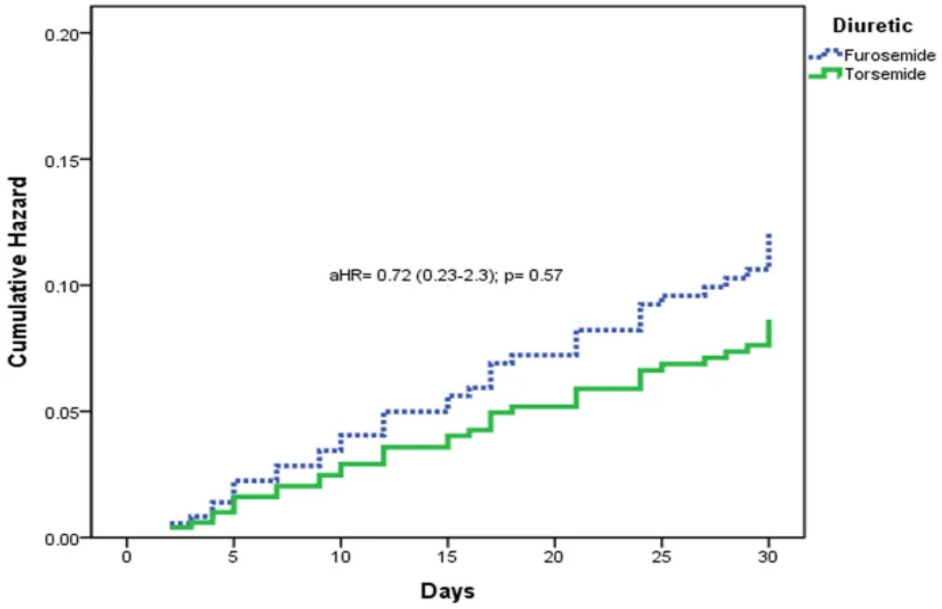

Figure 1: Outcome of both groups regarding hospital readdmission within one month.

Similarly, as shown in table 3 and figure 2, hospitalisation for HF within six months of discharge did not vary significantly between two groups.

Table 3: Comparison between both groups regarding hospital readmission

Outcome	Group 2	Group 1	Adjusted hazard ratio	P-value
Readmission within one month	14	62	0.72(0.32-2.3)	0.57
Readmission within 6 months	44	172	0.94(0.49-1.8)	0.87

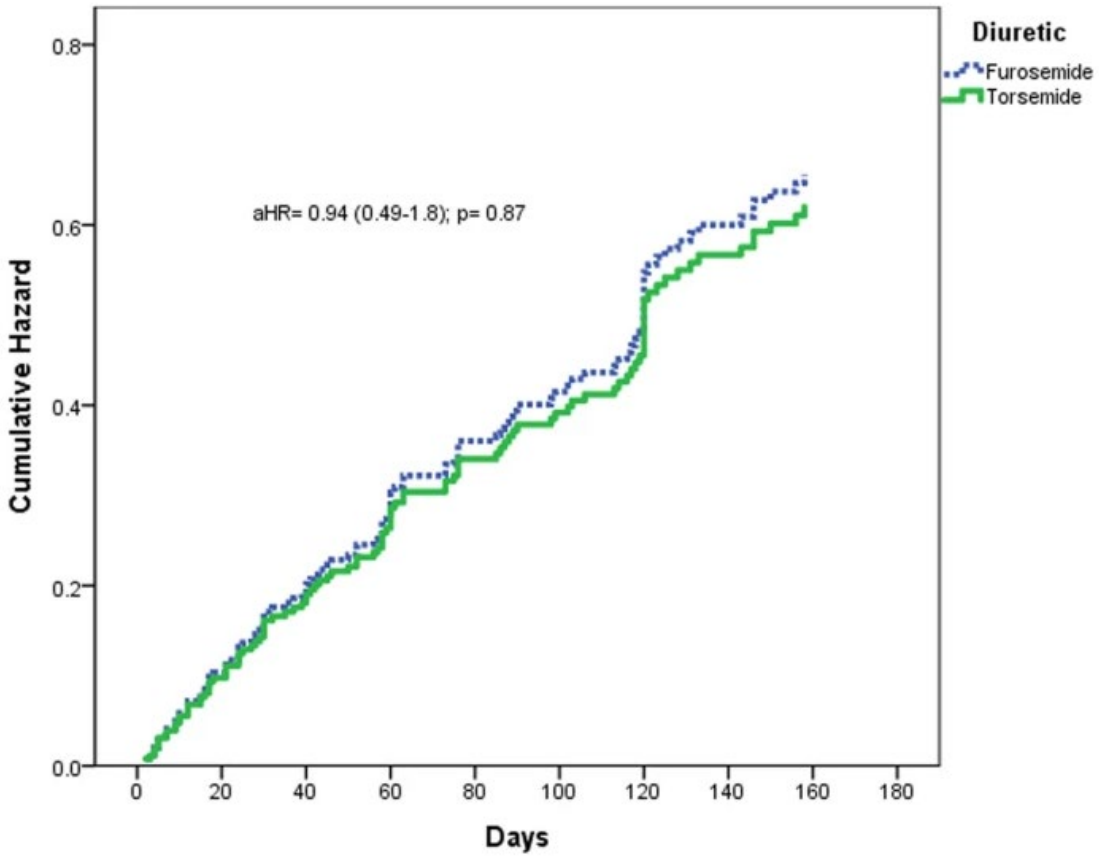

Figure 2: Figure 1: Outcome of both groups regarding hospital readdmission within 6 months.

Table 4 shows that aldosterone antagonist utilization increased the likelihood of prescribing torsemide. On the other hand, ACE inhibitors, ARBs, and age were negative predictors of torsemide usage.

Variables	**Adjusted OR**	**P-value**
ACE inhibitors or ARBs use	0.4	0.034
Aldosterone antagonists use	2.7	0.033
Age	0.97	0.065

OR: Odds ratio

Discussion

In the current study, switching furosemide to torsemide did not result in a decrease in hospitalisation due to heart failure in decompensated acute heart failure patients when compared to increasing the dose of furosemide within one month or six months follow-up.

Because torsemide has higher bioavailability and is more absorbed than furosemide in heart failure patients regardless the severity [3- 5- 8], it was predicted that shifting furosemide to torsemide would result in more favourable outcome and less hospitalization than increasing the dose of furosemide in decompensated heart failure patients who were already on furosemide before admission.

Two randomized clinical trials were included in a meta-analysis comparing furosemide and torsemide in patients with HF and revealed that torsemide reduces hospitalizations for HF. These two trials included individuals with chronic HF rather than decompensated HF [9].

Another large study evaluating mortality and morbidity following HF admission found that torsemide use resulted in a higher 30-day HF hospitalisation than furosemide, but after adjusting for clinical variables, torsemide use did not result in a higher 30-day HF hospitalisation than furosemide.Besides, this study did not assess switching from furosemide to torsemide[10].

Despite that torsemide has longer half-life and more bioavailability than furosemide that may favour its use, this study did not illustrate any beneficial effect in HF hospitalisation for torsemide over furosemide after one month and 6 months of follow up.

In this study,patients in group 1 were discharged on the baseline double dose, whereas those in group 2 were discharged on a torsemide dose equal to furosemide baseline dose, and there was no statistically significant variation in hospitalisation between the two groups.

As switching from furosemide to an equivalent torsemide dose have the same efficacy as increasing furosemide dose, this may indicate a therapeutic advantage of torsemide over furosemide.

We examined the factors that influence torsemide utilization in this study. Even though these associations may not necessarily suggest causality, they may represent a trend in prescription patterns or refer toward some indicators of disease progression to a stage where furosemide does

not achieve euvolemia desired level. Interestingly, our study, like Mentz et al.'s, revealed aldosterone antagonist as a positive predictor of torsemide utilization in HF and increasing age along with ACE inhibitor use as negative predictors [(10)].

This study has some limitations. First, it did not assess the effect of shifting torsemide to furosemide versus adjusting the dose of furosemide on mortality. However, a variation in mortality was not expected as placebo-controlled furosemide studies showed no difference. Second, while the results were adjusted for clinically significant variables, however, there is a potential for unmeasured or measured variables to influence these results. Third, the study overall patient population is quite small, which may have an effect on the results.

Conclusion

Shifting furosemide to an equivalent furosemide dose following acute decompensated heart failure did not result in a reduction in HF hospitalisation when compared to dose optimization of furosemide. As a result, clinicians may follow either strategy. However, larger longitudinal studies are essential to confirm these findings and to evaluate other critical cardiovascular outcomes, including mortality.

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