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Original research-Orijinal araştırma

Factors influencing the dose of loop diuretics in patients with systolic heart failure at discharge from the hospital

Sistolik kalp yetersizliği hastalarında hastaneden taburculukta reçete edilen kıvrım diüretiklerin dozunu etkileyen faktörler

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Abstract

Aim. Systolic heart failure (HF) is a chronic disease, associated with use of many drugs. Diuretics, particularly loop diuretics, are frequently prescribed to patients hospitalized with HF, and kept thereafter. However, diuretics are a group of drugs, which do not provide mortality benefit in HF, and, may bring about some risks, except in a specific group. Hence, it is important to understand the reasons driving physicians to use them. We retrospectively reviewed the hospital discharge records of HF patients. **Methods.** 700 patients with systolic HF were reviewed. Loop diuretic, furosemide, dose at disharge was classified into two categories as moderate-high (>40 mg/day) and low doses. **Results.** 613 patients were prescribed furosemide at discharge. Poor functional capacity (FC) (NYHA FC III-IV) at discharge (B=1.894), serum creatinine levels (B=1.567), and spironolactone prescription (B=2.427) were found to be independently associated with moderate-high dose of furosemide prescription during discharge. **Conclusion.** Diuretics are inevitable in systolic HF. Reasons driving the physicians to prescribe higher doses might be important in drawing pathways towards lower risks.

Key words: Systolic heart failure, loop diuretics, dose at discharge

Özet

Amaç. Sistolik kalp yetersizliği pek çok ilacın kullanıldığı kronik bir hastalıktır. Diüretikler, özellikle kıvrım diüretikleri, hastanaye yatırışan kalp yetersizliği hastalarına sıklıkla başlanır ve sonrasında devam ettirilir. Bununla birlikte diüretikler kalp yetersizliğinde mortalite faydası olmayan, bir özel grup haricinde bi takım riskleri beraberinde getiren ilaç grubudur. Bu yüzden hekimlerin neden bu ilaçlarını kullandıklarını anlamak önemlidir. Biz bu çalışmada kalp yetersizliği hastalarının hastaneden taburculuk raporlarını geriye doğru inceledik. **Yöntem.** Sistolik kalp yetersizliği olan 700 hasta gözden geçirildi kıvrım diüretiği, furosemid, hastane çıkışındaki dozu orta-yüksek (>40mg /gün) ve düşük doz şeklinde sınıflandırıldı. **Bulgular.** Taburculuk esnasında 613 hastaya furosemid reçetelenmişti. Çıkışta kötü fonksiyonel sınıf (NYHA FK III-IV) (B=1.894), kreatinin (B=1.567) ve spironolakton reçetelenmesi (B=2.427) çıkışta orta yüksek doz furosemid reçetelenmesi ile bağımsız ilişkili parametreler olarak bulundu. **Sonuç.** Diüretikler kalp yetersizliğinde kaçınılmaz ilaçlardır. Hekimleri yüksek doz reçetelemeye sevk eden nedenlerin anlaşılması, daha düşük riskli yollara yönelmek için önem olabilir.
Anahtar sözcükler: Sistolik kalp yetersizliği, kıvrım diüretikleri, taburculuk esnasındaki doz

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Introduction

Systolic heart failure (HF) is associated with increased mortality and morbidity [1]. Diuretics, with the exceptions of spironolactone and epleronone, are a group of drugs, which are inevitable for symptomatic improvement in patients with HF, though, they provide no benefit about mortality [2, 3]. While thiazide diuretics are reserved for those with hypertension and milder forms of HF, loop diuretics are the preferred form for patients hospitalized with congestive symptoms, due to their rapid onset of action and potency [4, 5]. Furthermore, most physicians continue to administer diuretics after treatment of congestion for the purpose of maintaining dry weight and salt homeostasis. On the other hand, continued use of diuretics in patients with HF may be detrimental due to neurohormonal activation or electrolyte imbalance [6]. Furthermore, empirical outpatient loop diuretic dose was shown to be independently associated with increased mortality in patients with HF [7]. Choosing either high dose or low dose diuretics during discharge after relief of congestion in patients with HF might be important in avoiding the potential risks of them. We reviewed the patients who were hospitalized with the diagnosis of systolic HF, and aimed to evaluate factors associated with prescription of high dose loop diuretics (furosemide, >40 mg/day, p.o) during discharge from the hospital.

Materials and methods

Hospital discharge records of consecutive 700 (491 male, 209 female) patients who were hospitalized with acutely decompensated systolic heart failure, were reviewed. Total daily dose of furosemide at discharge was considered, and classified into two categories named as >40mg/day (Group 1, moderate-high dose) or less than and equal to 40 mg/day (Group 2, low dose). BUN, creatinine, haemoglobin levels at discharge were considered along with other discharge prescriptions. Those with ejection fraction (EF) >45% were not included.

Statistical Analysis:

Parametric data were expressed as mean ± standard deviation, and categorical data as percentages. SPSS 10.0 was used to perform statistical procedures. Independent parameters were compared according to Independent sample's t test. Categorical data were evaluated by chi square test as appropriate. Multivariable logistic regression was used to evaluate independent parameters affecting discharge dose of furosemide. A p value of ≤ 0.05 was accepted significant.

Results

Mean age was 57±15 years, mean EF 34±7%, and median functional class (NYHA) was III as a whole group. Loop diuretics (furosemide was the only form in all cases) were prescribed to 87.6% (n=613) of discharged patients with heart failure. Of note, no patient was reported to have congestion at discharge. Mean furosemide dose in Group 1 was 83±12 mg/day, and in Group 2 was 34±10 mg/day. Investigated parameters with regard to the dose of furosemide were presented in Table 1. Serum creatinine was significantly higher in Group 1 (n=78) than in Group 2 (n=535) (1.4±1.2 vs.1.1±0.5 mg/dl, p=0.033). Furthermore, serum creatinine was modestly, but, significantly correlated with dose of furosemide at discharge (r=0.157, p<0.001). Ejection fraction was significantly lower in Group 1 than in Group 2 (p=0.049, Table 1). Diabetes mellitus was present in 29.5 % of Group 1, and 15% of Group 2 (p=0.002). ACE inhibitor prescription was associated with use of low dose furosemide (p=0.024). In those patients prescribed spironolactone, irrespective of dose (25 mg/day in most of the cases), during discharge, moderate-high dose was present in 14.5% of all, whereas, in those who were not prescribed spironolactone, moderate-high dose was present in only 6.6% (p=0.015). Prescription of spironolactone increased the likelihood of prescription of moderate-high dose furosemide by 2.386 folds (Odds ratio, 95% confidence interval 1.159-4.916). When NYHA functional class (FC) was classified into two categories named as FC I-II and III-IV, it

was noticed that moderate-high dose during discharge was present in 17.5% of those patients with FC III-IV during discharge, whereas, 9% of those with FC I-II (p=0.002). Having poor FC at discharge increased the likelihood of prescription of moderate-high dose furosemide by 2.154 folds (Odds ratio, 95% confidence interval 1.326-3.499).

Parameters, found to be significantly different (Table 1, p<0.1) in univariate analysis were enrolled into multivariable logistic regression analysis. It was found that (Figure 1) poor FC (NYHA FC III-IV) at discharge (FC III-IV) (p=0.013, B=1.894, 95% confidence interval 1.146-3.128), higher creatinine (p=0.006, B=1.567, 95% confidence interval 1.141-2.152), and spironolactone prescription (p=0.0022, B=2.427, 95% confidence interval 1.135-5.190) were found to be independently associated with moderate-high dose of furosemide prescription at discharge.

Table 1: Comparison of parameters between moderate-high dose versus low dose furosemide.

	Group 1 (n=78)	Group 2 (n=535)	p
Age (years)	56±17	57±15	0.472
Sex (male/female)	60/18	372/163	0.181
Ejection fraction (%)	32±8	34±7	0.049
NYHA III/IV vs II	47/31	221/314	0.002
Etiology (ischemic versus nonischemic)	54/24	239/296	<0.001
Hemoglobin (gr/dl)	12.3±1.8	13.4±5.1	0.06
BUN (mg/dl)	35.9±18.2	26.3±15.5	<0.001
Creatinine (mg/dl)	1.4±1.2	1.1±0.5	0.033
Diabetes mellitus	23/78 (29.5%)	80/535 (15%)	0.002
Hypertension	17/78 (21.8%)	155/535 (29%)	0.237
ACE inhibitor	65/78 (83.3%)	489/535 (91.4%)	0.024
ARB	8/78 (10.3%)	28/535 (5.2%)	0.115
Hydrochlorothiazide*	57/78 (73.1%)	438/535 (81.9%)	0.066
Spironolactone	69/78 (88.5%)	408/535 (76.3%)	0.015
Digoxin	58/78 (74.4%)	429/535 (80.2%)	0.298

ACE: angiotensin receptor antagonist, ARB: Angiotensin II receptor blocker, *available in plus forms inside ACE inhibitors or ARBs

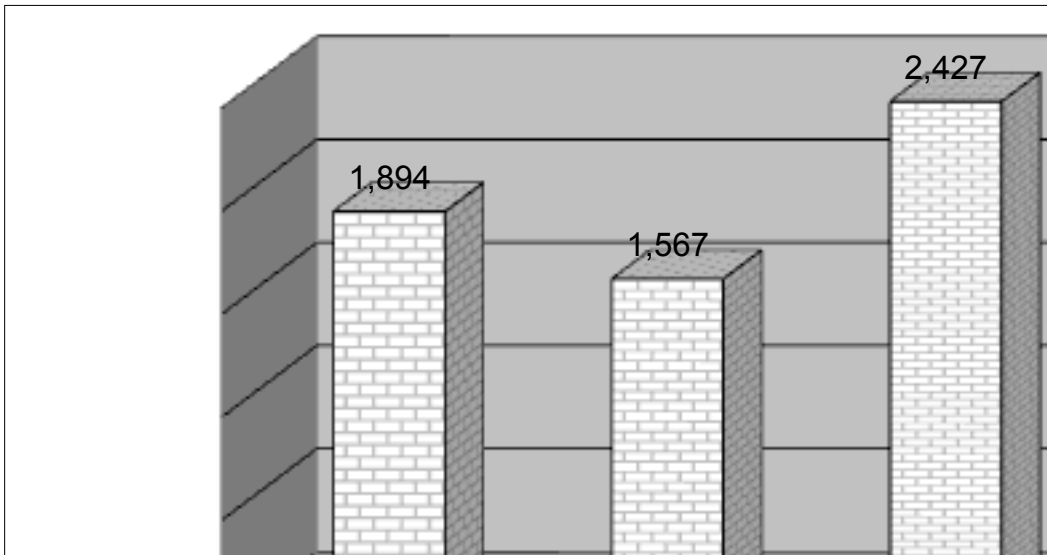

Figure 1: Odds of independent risk factors, found in multivariable regression analysis, for prescription of high dose loop diuretic at discharge.

Discussion

Diuretics are inevitable for congested patients with HF, and have been used worldwide. Considering acute hemodynamic actions, diuretics provide immediate direct or indirect vascular actions, diuresis and volume redistribution [8]. On the other hand, continuous use of diuretics may potentially be hazardous leading to neurohormonal activation [9-11]. Furthermore, outpatient high dose diuretic therapy was shown to increase mortality in patients with HF by several folds after adjusting for multiple factors [7]. Besides, there is evidence that use of non-potassium-sparing diuretics was associated with a significantly increased incidence of sudden, arrhythmic death, contrary to potassium sparing ones [12, 13]. However, simply due to lack of reasonable alternative for the control of congestive symptoms, they have been accepted as first line therapy in the management of patients with HF. Since, it was shown that it was possible to decrease the outpatient dose of diuretics to one third of initial dose in HF patients, who were clinically stabilized with high doses of diuretics [14], it seems critical to know about the factors associated with the prescription of high dose diuretics at discharge in order to avoid some negative outcomes, associated with use of them.

In our study, we found that patients with lower EF and higher creatinine were prescribed higher doses of furosemide empirically at discharge despite absence of congestion. On the other hand, in high dose diuretic group, there were more patients with diabetes mellitus, which was associated with both poorer renal function, and EF, though not significant, compared to nondiabetic patients (p=0.175, p=0.105). Patients in high dose diuretic had poorer NYHA at discharge and hence, prescribed spironolactone more frequently, in accordance with the guidelines [15]. Of note, poor NYHA functional class at discharge, higher creatinine, and prescription of spironolactone at discharge were independent predictors of high dose diuretics at discharge prescription. The reasons driving physicians to prescribe high dose diuretics in these patients remains to be established.

Our study was limited by its retrospective nature, and hence, there might exist many confounders. Some parameters such as blood electrolytes at discharge, data regarding ICD/CRT implantation could not be evaluated simply due to reporting problems. Besides, this study presents data about a single tertiary care centre. Hence, the results should not be extrapolated to all centres. On the other hand, lack of availability of other loop diuretics in our country also limits our conclusions. However, we think that tendencies responsible for empirical prescription of furosemide, one of the most frequently preferred loop diuretics, might provide clinicians with the understanding of avoidance of unnecessarily high dose prescription to some extent, and also might help understanding use of diuretics with high doses on the basis of fluid status for short periods.

Diuretics are inevitable in systolic HF, and are added to prescriptions empirically in most of the patients during discharge from the hospital. It is reasonable to avoid negative consequences by decreasing unnecessary use of these drugs. On the other hand, reasons driving the physicians to prescribe higher doses of diuretics might be important in drawing pathways towards lower risks.

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