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Research Article

ALTERATION IN RENAL FUNCTION FOLLOWING LOOP DIURETICS IN PATIENTS WITH ACUTE DECOMPENSATED HEART FAILURE

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ABSTRACT

Objective: The objective of the study was to monitor the impact of loop diuretic therapy in patients with acute decompensated heart failure (ADHF) and to assess other predictors of renal dysfunction in patients with ADHF.

Methods: An observational study over a period of 6 months from January 2018 to June 2018 in the Department of Cardiology, in a Tertiary Care Teaching Hospital, Coimbatore, Tamil Nadu. Patients on diuretic therapy (loop diuretic) were enrolled. Patients with prior chronic kidney disease were excluded from the study. The patients were evaluated based on change in serum creatinine (SCr) and other contributing factors were assessed by acute kidney injury network and worsening of renal function criteria.

Results: A total of 135 patients were enrolled, of which 73% were males and 27% were females. The mean age of the subjects was 61.55±13 years. The baseline means SCr was 1.62±0.92 mg/dl. On evaluation, 41% were really affected and 59% remain unaffected. Factors such as hypertension (p=0.047) and angiotensin-converting enzyme inhibitors (ACE-I) (p=0.023) were found to be significant predictors of renal injury.

Conclusion: Variation in renal function in ADHF patients was multifactorial. The direct influence of loop diuretics on renal function was present but was not well established. Hypertension and ACE-I have found to show influence in the development of renal injury as contributing factors. There exists both positive and negative consequence of loop diuretics on renal function.

Keywords: Acute decompensated heart failure, Loop diuretics, Renal dysfunction, Serum creatinine.

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INTRODUCTION

Acute decompensated heart failure (ADHF) is a clinical syndrome of new or worsening signs and symptoms of HF, often leading to prolonged hospitalization or a visit to the emergency department [1]. Patients hospitalized for ADHF often develop worsening renal function which occurs in 25–30% [2]. Acute worsening of renal function (WRF) is one of the commonly observed clinical scenarios in ADHF [3]. Loop diuretics serve as a cornerstone therapy in ADHF to manage congestion [4,5]. The link between loop diuretic and renal changes is bidirectional; it can either improve or worsen renal function. Uncertainty exists about the safety and efficacy of various doses and an unknown relationship between loop diuretics and WRF [6]. Various other factors have impact on renal dysfunction, but the extent of influence of a particular factor is unknown. This study focuses on the impact of diuretics and the factors that additionally contribute to the variation in renal function.

METHODS

A prospective observational study was conducted for a period of 6 months from January 2018 to June 2018 in the department of cardiology of a tertiary care hospital, India. The study was approved by the Institutional Human Ethical Committee. All ADHF patients receiving loop diuretics were included in the study. Patients who had a prior history of chronic kidney disease were excluded from the study as it focuses on newly developed renal dysfunction. Data were collected from inpatient case sheets and hospital information system (HIS). The study population was categorized based on acute kidney injury network and WRF criteria for the analysis of factors.

Demographic variables were reported as mean±SD. Paired *t*-test was used to estimate the association between the baseline serum creatinine (SCr) and SCr at discharge.

One way ANOVA test was used to assess the association of factors like comorbidities and coadministered medications with renal function. All analysis was performed using Statistical Package for Social Sciences Version 16.0.

RESULTS

During the study period, 135 patients on loop diuretics were enrolled, of which 73% were males and 27% were females. The mean age of subjects was 61.55±13 years (Table 1). Baseline SCr was recorded to assess the degree of renal function on admission. Based on the elevation of SCr from the baseline, 41% were really affected and 59% remain unaffected. SCr values at the baseline and after 48 h of loop diuretic administration were analyzed. The mean of the baseline SCr was 1.62±0.92 mg/dl and the mean of rise in SCr after 48 h was 0.67±0.84 mg/dl.

After the administration of loop diuretics, 41% of the population developed renal injury. The SCr levels were monitored to assess the

Table 1: Patient demographics

Demographics	n=135 (%)	*p value
Age (years)	61.55±13	0.163
Gender		
Male	102 (73)	0.032
Female	32 (27)	

n=135, *Significant p value (<0.05).

Table 2: Factors that influence renal dysfunction

Factors	AKIN			WRF		
	AKI (n=12) %	Non-AKI (n=20) %	*p value	WRF (n=43) %	non-WRF (n=60) %	*p value
Comorbidities						
Diabetes mellitus	9 (47)	10 (53)	0.205	28 (43)	37 (57)	0.167
Hypertension	7 (64)	4 (36)	**0.010**	30 (48)	32 (52)	**0.045**
Heart disease	9 (41)	13 (59)	0.934	23 (38)	37 (62)	0.314
Anemia	4 (33)	8 (67)	0.454	8 (44)	10 (56)	0.385
rEF <40	11 (46)	13 (54)	0.352	22 (36)	39 (64)	0.568
pEF >40	3 (30)	7 (70)	0.552	19 (48)	21 (52)	0.453
Pedal edema	3 (20)	12 (80)	0.038	11 (38)	18 (62)	0.489
In-hospital medications						
ACE-inhibitors	11 (52)	10 (48)	**0.005**	13 (30)	30 (70)	**0.030**
ARBs	4 (100)	0 (0)	0.010	4 (25)	12 (75)	0.169
Beta-blockers	9 (56)	7 (44)	0.934	18 (44)	23 (56)	0.314
Metolazone	8 (31)	18 (69)	0.643	4 (50)	4 (50)	0.218
Calcium channel blockers	4 (80)	1 (20)	0.059	8 (42)	11 (58)	0.769
Inotropes	2 (50)	2 (50)	0.845	11 (55)	9 (45)	0.561

n=135, *Significant p value (<0.05). pEF: Preserved ejection fraction, rEF: Reserved ejection fraction, ARB: Angiotensin receptor blocker, ACE: Angiotensin-converting enzyme, AKIN: Acute kidney injury network, WRF: Worsening of renal function

renal function until discharge. The decrease SCr in was observed in 76% of population which was statistically significant (*p=0.003). It was found that elevated SCr after loop diuretic administration will improve later. However, 24% of the population who developed renal injury after loop diuretic therapy had persistent elevation of SCr.

On further evaluation of the reason behind the occurrence of renal injury, it was inferred that various factors such as comorbidities and coadministered medications had an impact on renal impairment. Hypertension (*p=0.010) and angiotensin-converting enzyme inhibitors (ACE-I) (*p=0.005) were found to have a significant impact on WRF (Table 2). This elucidated that hypertension and ACE-I are the contributing elements for renal impairment.

DISCUSSION

Over the years, renal dysfunction has been a common complication for ADHF patients. It is shown that loop diuretics have an association with worsening renal function [7]. The time to develop AKI is important, as SCr levels change at different stages of admission. During the first few days of admission for ADHF, elevation in SCr reflects cardiorenal syndrome [8], characterized by various mechanisms like renal hypoperfusion, renal venous congestion, and associated activation of cytokine and neurohormonal axes [9].

Current clinical practice exhibits a short term rise in SCr post loop diuretic therapy. It acutely causes a decrease in the estimated glomerular filtration rate (eGFR) which often leads to renal injury [10]. Worsening renal function was developed in 25–30% of the population with ADHF [2]. The cause of the incidence was unclear. In the present study, 41% of the population receiving loop diuretics developed renal impairment. Similarly, a study portrayed the use of loop diuretics was associated with a slightly greater rate of decline in eGFR [11]. Therefore, an average of 35% of patients with ADHF on loop diuretics has a possibility of developing renal injury.

Among the patients with renal dysfunction, 76% improved at the time of discharge. It depicts that the progress of the condition was owing to the control of the disease [12]. The magnitude of dose variation among individuals was dependent on the clinical condition of the patients. Changes in the dose of diuretics were not taken into account for analysis.

The worsening picture of renal function does not merely depend on loop diuretic therapy which was similarly addressed by El-Refai *et al*. in a cohort study of 6071 patients, who estimated a plausible relation between day and day change in SCr with loop diuretics exposure, which denoted that loop diuretic did not have a large clinical impact on renal function [13]. However, 24% of the population who developed renal injury after loop diuretic therapy had persistent elevation of SCr. The study could not confirm that the development of renal injury was solely dependent on loop diuretics. The reason remains hypothetical, which led to the assessment of factors to figure out the correspondence.

Many studies evaluated the association of different predictors such as age, ejection fraction, comorbidities, and coadministered medications in the occurrence of AKI in ADHF patients [14-16]. The present study indicated age-related systemic effects were not correlated to the onset of renal dysfunction. ADHERE registry, an epidemiological survey showed the prevalence of hypertension serves as a risk factor for the worsening of kidney function and is approximated around 68% [17]. The recent clinical study elaborated that hypertensive renal injury correlates most strongly with elevated pressure [18].

Correlates most strongly with elevated pressure. It was found that hypertension (p=0.01) was associated with renal impairment, whereas the other comorbid conditions were not statistically significant. Another study illustrated that diabetes, elevated systolic blood pressure, history of HF, tachycardia, and female gender were associated with the risk of WRF [8].

Another aspect of critical importance is regarding coprescribed medications. The impact of medications which included ACE-I, angiotensin receptor blockers (ARBs), beta-blockers, metolazone, calcium channel blockers, and inotropes was analyzed based on their potential renal effects. Well-designed clinical trials have demonstrated that ACE-I and ARBs are able to preserve renal function [19]. ACE-I had an add-on effect in renal dysfunction when combined with loop diuretics. Similar inferences were deduced from a study that describes the effect of ACE-I and ARB associated with cardiorenal risk which is likely to vary individually [20].

Therefore, disease progression along with the factors mentioned above is likely the reason for the persistence of renal injury by which loop diuretics may have its indirect effects. Furthermore, a detailed evaluation of individual patients with additional key determinants such as markers and extended sample size is required to predict the occurrence of AKI with diuretic therapy.

CONCLUSION

Variation in renal function in ADHF patients was multifactorial. The direct influence of loop diuretics on renal function was present but was not well established. Hypertension and ACE-I showed influence in the development of renal injury as contributing factors. There exists both

positive and negative consequence of loop diuretics on renal function. Therefore, a more detailed evaluation of individual patients with additional key determinants such as markers and extended sample size is required to assess the WRF.

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AUTHORS' CONTRIBUTIONS

All the authors have contributed equally to the design, development, review, and finalization of the contents of the manuscript.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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