A STUDY OF HIGH DOSE VERSUS LOW DOSE FUROSEMIDE THERAPY IN PATIENTS WITH ACUTE DECOMPENSATED HEART FAILURE

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ABSTRACT

BACKGROUND

In cases of Acute Decompensated Heart Failure (ADHF) Loop diuretics are an important component of current treatment and are administered to approximately 90% of patients who are hospitalized with heart failure[1]. Despite decades of clinical experience with these agents, there are few studies to guide their use.

MATERIALS AND METHODS

Total 60 patients included in the study (30 in each group), were randomized into two groups – High dose and Low dose furosemide therapy group. Following were considered as the end points, negative fluid balance at 24 hours after admission, duration of hospital stay, trend of serum electrolytes, clinical outcome (death and hospital re-admission).

RESULTS

We noticed that there was significant diuresis in the first 24 hours and shorter hospital stay in high dose diuretic group. There was no significant difference in serum sodium and potassium levels and hospital re-admission. There was significant difference in the renal parameters with transient elevation in serum urea and creatinine, seen in high dose group as compared to low dose group.

CONCLUSION

Both high dose and low dose diuretic modality of treatment have equal role in the management of ADHF. High dose diuretic strategy has been associated with shorter hospital stay and rapid improvement in clinical symptoms so, it might be effective diuretic strategy.

KEYWORDS

High dose furosemide, Low dose furosemide, ADHF, Heart failure therapy.

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BACKGROUND

Loop diuretics are the important modality of treatment in patients with Acute Decompensated Heart Failure (ADHF).[1] Though diuretics form an important modality of treatment, there are very sparse studies regarding the guidance of the therapy and most of present guidelines are depends on the opinion of experts.[2,3] Administration of loop diuretics to patients with heart failure has been shown to activate the Renin-Angiotensin-Aldosterone System (RAAS) and the Sympathetic Nervous System (SNS), electrolyte disturbances, and worsening of renal function.[4] In addition, observational studies have shown associations between high doses of diuretics and adverse clinical outcomes, including renal failure, progression of heart failure, and death.[5-7] Loop diuretics have their effect on renal parameters, serum electrolytes, splanchnic blood flow and drugs metabolism so there will be variable response in ADHF.[8-9] Administration of loop diuretics may lead to electrolyte imbalances (such hypokalaemia, hyponatremia) that may exacerbate cardiac arrhythmias and increase the risk of sudden cardiac death. We sought to determine if there are any differences in clinical outcomes between intravenous High dose and Low dose of loop diuretics.

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Aim

To study the various diuretic strategies in patients with Acute Decompensated Heart Failure.

MATERIALS AND METHODS

Patients with Age more than 18 year and prior clinical diagnosis of heart failure (HF) on daily home use of oral loop diuretic for at least one month and who were identified within 18 h of hospital admission were included in the study. Patients with systolic BP <80 mm Hg and serum creatinine >3.50 mg/dl at baseline were excluded.

Study Design

This was a prospective, randomized, double-blind study comparing High Dose versus Low dose of furosemide in patients of ADHF. Patients who were diagnosed with ADHF were initially taken written and informed consent for study treatment and data collection was obtained from each patient. At the time of admission patient's clinical symptoms and signs of heart failure were noted – paroxysmal nocturnal dyspnea, orthopnoea, pedal oedema, ascites, blood pressure, and jugular venous pressure were noted. Patient's baseline clinical data and previous drugs intake listed. Cases were randomized into two groups - "Low Dose" furosemide therapy (1 × chronic oral dose) and "High Dose" furosemide therapy (2.5 × chronic oral dose) in patients with ADHF. We assessed urine output at 24-hour at bedside, length of hospital stay, serial serum electrolytes and renal parameters were noted. We also assessed one-month clinical outcome (Death and Emergency Department visits).

Statistical Analysis

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS

Overall 60 patients were enrolled in the study. The baseline clinical data are summarized in Table 1.

	Total		High dose		Low dose		P value
	Count	%	Count	%	Count	%	
Age (years) Mean ± SD	56.25 ± 9.7		57.4 ± 9.9		55.1 ± 9.6		0.365
Male	39	65%	20	66.7%	19	63.3%	0.787
Diabetes	38	63.3%	22	73.3%	16	53.3%	0.145
Hypertension	48	80%	25	83.3%	23	76.7%	0.713
Dyspnea or Orthopnoea Day 1	49	81.6%	26	86.7%	23	76.7%	0.317
Oedema	40	66.6%	25	83.3%	15	50.0%	0.006*
Rales	38	63.3%	19	63.3%	19	63.3%	1.000
JVP	49	81.6%	30	100.0%	19	63.3%	<0.001*
Antiplatelet	16	26.7%	6	20.0%	10	33.3%	0.306
Angiotensin converting enzyme inhibitors	41	68.3%	22	73.3%	19	63.3%	0.544
Beta blockers	31	51.7%	17	56.7%	14	46.7%	0.571
Spironolactone	23	38.3%	11	36.7%	12	40.0%	0.564
Pulse (beats per minute)	111.2 ± 9.9		109.5 ± 8.9		113 ± 10.8		0.184
Systolic BP (mmHg)	151.3 ± 9.5		152.4 ± 9.5		150.2 ± 9.7		0.378
Diastolic BP (mmHg)	90.3 ± 5.4		91.2 ± 6.1		89.5 ± 4.8		0.233

Table 1. Demographic and Baseline Profile of the Patients Among two Groups

The median total dose of loop diuretics received over the course of 72 hours was 256 mg with the low dose strategy as compared with 614mg in high dose strategy. Majority of the patients were males (65.0%). Most of them had high risk features such as hypertension (80%), diabetes (62%). Dyspnoea and orthopnoea was the most common presentation (81.7%). There was no statistically significant difference between the two groups of patients regarding demographics, risk factors and symptoms.

In the study mean duration of hospital stay in High dose group was 8.6 ± 1.7 days and in Low group was 12.8 ± 2.4 days. This difference in duration of hospital stay was statistically significant.

			Day 1	Day 3	Day 7
Urea	High Dose	Mean	41.9	39.1	43.4
		SD	4.4	8.1	3.6
	Low Dose	Mean	35.6	34.5	35.4
		SD	9.3	9.2	9.6
P Value			<0.002*	<0.045*	<0.001*
Creatinine	High Dose	Mean	1.4	1.3	1.3
		SD	0.2	0.2	0.2
	Low Dose	Mean	1.4	1.3	1.3
		SD	0.4	0.3	0.3
P Value			0.848	0.799	0.972

Table 2. Comparison of Serum Urea and Creatinine between two Groups at Different Time Intervals

In the study there was no significant difference in serum sodium and potassium levels between two groups. Mean Creatinine in high dose group on day 1 was 1.4 ± 0.2 and in low dose group was 1.4 ± 0.4. This difference in mean Creatinine on day 1 between two groups was statistically significant. On other days of follow up there was no significant difference in mean Creatinine between two groups. In the study Mean Blood Urea was higher in High dose group compared to Low dose group at all the intervals of follow-up. This difference in Mean blood urea was statistically significant at all the intervals. (Table 2)

Urine Output	Group				P value
	High dose		Low dose		
	Mean	SD	Mean	SD	
Till 24 hr	1130.6	133.4	759.5	40.7	<0.001*
24 to 48 hr	930.6	337.5	880.3	47.4	0.423
48 to 72 hours	915.2	195.6	903.6	51.7	0.755

Table 3. Comparison of Urine Output Between Two Groups at Different Time Interval During Follow-up

In the study Mean Urine output was significantly higher in High dose on day 1, day 2 and day 3 compared to low dose group. This difference in mean urine output between two groups till 24 hrs was statistically significant. (Table 3)

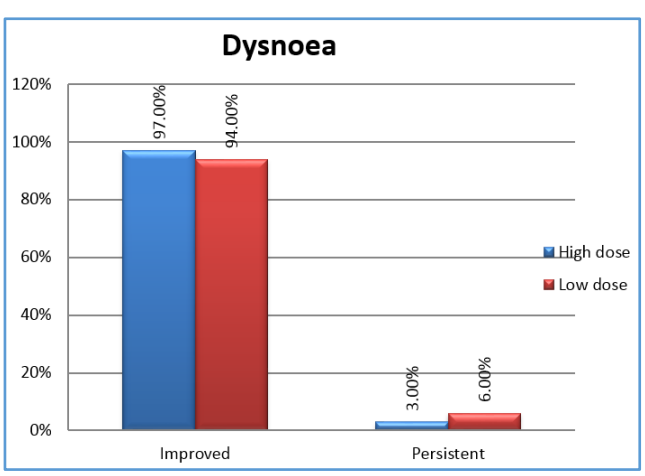

Figure 1. Comparison Improvement of Dyspnoea between Two Groups on 3rd Day of Follow up

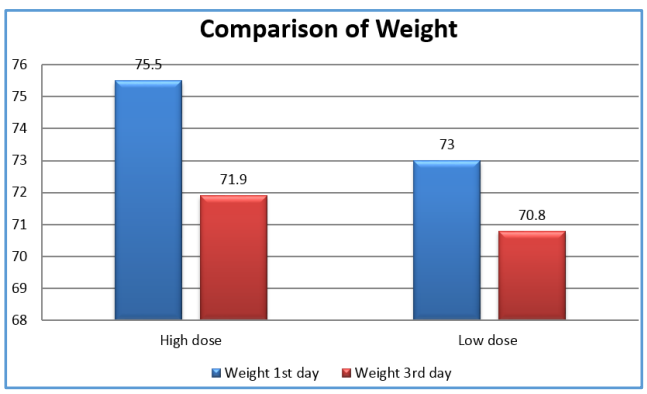

Figure 2. Comparison of Improvement of Weight between Two Groups on 3rd Day of Follow up

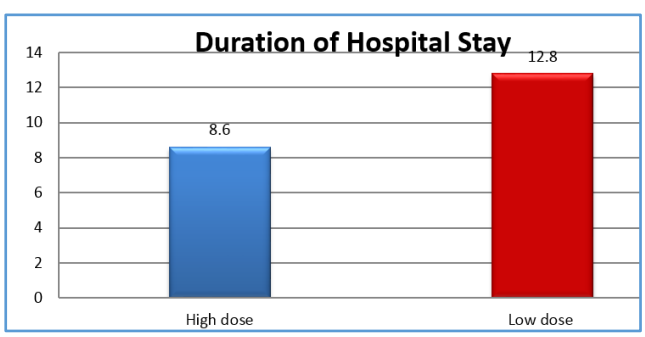

Figure 3. Comparison of Duration Of Hospital Stay Between Two Groups

In this study we noticed that 36.7% of high dose group and 46.7% of low dose group required readmission during follow up.

DISCUSSION

ADHF is associated with pulmonary congestion and volume overload with high morbidity and mortality. Loop diuretics are an essential component of therapy for acute decompensated heart failure, there have been few prospective data to guide decision-making regarding the use of these agents.

In our study we noticed that there was, (1) More diuresis in the first 24 h and hospital stay was short with the High dose, (2) No statistical difference in serum sodium or serum potassium levels between the groups and 3) Transient elevation of renal parameters in High dose therapy group.

There was a more loss of fluid in the High dose group as compared to Low dose group. This could be because of a faster initial diuresis in high dose group. The High -dose strategy was associated with greater relief of dyspnoea, greater fluid loss and weight loss. This is in accordance to the study conducted by G. Michael Felker, M.D et al, who also noticed that high-dose strategy was associated with greater relief of dyspnoea, greater fluid loss and weight loss, and fewer serious adverse events[7]. Another study by Metra M et al noticed that patients with ADHF with early and faster relief of dyspnoea were associated with more favourable outcomes after discharge from the hospital.[8]

We noted in our study that there was no statistically significant difference in serum sodium, serum potassium between two groups, this is in accordance to DOSE trial where they concluded that, no significant difference in the Serum electrolytes between two groups.[9]

In our study we noticed that significant increase in blood urea and creatinine level between two groups at different intervals of follow up, this is in accordance to Butler J, et al suggested that high doses of diuretic had been associated with Transient worsening of renal function,[10] which has been proposed as a mechanism by which loop diuretics could lead to worse outcomes.[11]Felker, M.D et al also noticed transient worsening of renal function with the high dose strategy as compared to low dose strategy. Aronson D et al and Testani JM et al, also observed in their study that, transient worsening of renal function with high dose strategy for heart failure may not affect the outcomes after discharge from the hospital.[11,12]

In our study, we noted that there was shorter hospital stay among the High dose group. This could be because of rapid initial diuresis, as patients get relief from the congestion and overload status early probably leading to and so there was shorter hospital stay. However, other studies showed different results. In DOSE trial[13] the length of hospital stay was similar in bolus and infusion group (mean of 5 days; p = 0.97).

The number of emergency visits to the hospital for recurrent HF within the first month of discharge was not significant among the two groups. We had one deaths in the High dose group and one in the Low dose group during the one month follow up.

CONCLUSION

Both high dose and low dose diuretic modality of treatment have equal role in the management of ADHF. High dose diuretic strategy has been associated with shorter hospital stay and rapid improvement in clinical symptoms so, it might be effective diuretic strategy.

Limitations

1. This was a single centre study with a small sample size.
2. We considered blood urea and serum creatinine as measures to see for worsening renal function. Patient baseline weight and e-GFR could not be determined as patients were clinically unstable.

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