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Editorial

Diuretic therapy in acute decompensated heart failure – Bolus or continuous?

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The combination of aging of the population and improved survival after myocardial infarction has created a rapid rise in the number of patients currently living with chronic heart failure, with a consequent increase in the number of hospitalizations for acute decompensated heart failure.

Congestion and volume overload are the hallmarks of acute decompensated heart failure (ADHF), and loop diuretics have historically been the cornerstone of the therapy. Diuretic therapy is the standard treatment in emergency rooms and in the cardiac intensive care units. Loop diuretics in the form of bolus doses are given for the symptomatic relief of acute onset of breathlessness. In patients with pulmonary edema, fluid restriction and diuretic therapy have been shown to promote a faster resolution of symptoms and clinical improvement, and have also been associated with a decrease in the duration of stay in the intensive care unit.[1]

Among the loop diuretics, Furosemide and Torsemide are the most commonly used for the management of acute decompensated heart failure. They result in brisk diuresis and the property of mild peripheral venodilation helps in further reduction of preload. Hence, they relieve symptom of breathlessness in patients with volume overload presenting as ADHF.[2]

Their mode of administration is either as bolus doses or continuous infusion. Several reports have suggested that continuous intravenous administration of loop diuretics may be superior to intermittent administration.[3] Till today, we do not have a consensus about the mode of administration of diuretic treatment in these patients. There are many small observational studies comparing bolus doses with continuous infusion of diuretics in ADHF management. They had conflicting results. Aziz et al evaluated 116 patients retrospectively and divided them into two groups: Group A patients received furosemide by continuous infusion combined with low-dose dopamine infusion. Group B patients received bolus therapy of intravenous furosemide. The effect on renal function and re-admission rate was recorded.[3] They concluded that continuous infusion of furosemide in addition to low-dose dopamine is safe, effective and less nephrotoxic than intermittent boluses in patients admitted with acute decompensated heart failure and associated with shorter hospital stay with lower readmission rates at 30 days.

One study that deserves to be specifically mentioned in this context is the DOSE study by Felkar et al In this trial, they compared bolus versus infusion and high dose versus low dose of furosemide. There was no difference in the net fluid loss at 72 h in bolus versus continuous infusion arms, but high dose group had greater diuresis than low dose group. As per the DOSE study, among patients with acute decompensated heart failure, there were no significant differences in patients' global assessment of symptoms or in the change in renal function when diuretic therapy was administered by bolus as compared with continuous infusion or at a high dose as compared with a low dose.[4] Those who have severe breathlessness have better symptom relief by higher intravenous intermittent bolus doses. As per the results of DOSE study, higher doses of diuretics may offer clinical advantages in terms of greater diuresis, weight loss, and relief of dyspnea, without any identified long-term disadvantages.[4]

Some of the trials and meta-analyses which are listed in Table 1, did not show any consensus about the use of diuretic therapy and its mode of administration.

In their meta-analysis, Amer et al have concluded that furosemide given as a continuous infusion leads to greater diuresis and reduction in body weight in pts admitted for ADHF compared to bolus doses. Urinary Sodium excretion and duration of hospital stay did not differ between the two groups.[13]

In this issue of the Indian heart journal, Shah et al have presented their elegantly conducted study of comparison of

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Table 1 – Randomized Trials of Bolus Versus Continuous Infusion of Diuretics in Heart Failure Study [Updated table adapted with permission from Felker GM, O'Connor CM, Braunwald E. *Circ Heart Fail*. 2009 Jan; 2(1):56–62.].

Study	No. of patients	Design	Intervention	Duration	Endpoints	Findings
User at al[5]	8	Randomized, cross-over, unblinded	Continuous infusion vs BID IV bolus	24 h	Urine output	Bolus better
Dormans et al[6]	20	Randomized, cross-over, unblinded	Continuous infusion vs single IV Bolus	24 h	Urine output	Infusion better
Kramer et al[7]	8	Randomized, cross-over, unblinded	Continuous infusion vs single IV 24 h Bolus	24 h	Urine output	No difference
Lahav et al[8]	9	Randomized, cross-over, unblinded	Continuous infusion vs Q8 bolus	48 h	Urine output	Infusion better
Licata et al[9]	107	Randomized, single blind	Continuous infusion + hypertonic saline vs Q12 bolus	6-12 days	Urine output at 24 h & Mortality	Infusion better on all end points
Bivouac et al[10]	20	Randomized, single blind, crossover	Q12 4-h infusion vs Q12 bolus	24 h	Urine output	Infusion better
Schuller et al[11]	33	Randomized, unblinded	Continuous infusion vs bolus IV BID	72 h	Mortality	No difference
Shah et al[12]	308	2 × 2 factorial design Randomized clinical trial	Continuous infusion bolus IV BID	24 h	Symptom relief, renal function, net fluid loss, or death and rehospitalization at 60 days	Patients on higher diuretic doses have greater disease severity, and may benefit from an initial bolus strategy
Aziz et al[3]	116	Retrospective analysis	Continuous infusion combined with low-dose dopamine infusion vs. bolus therapy	48 h	Nephrotoxicity, determined by the rise in blood urea nitrogen and creatinine levels, and readmission rates for heart failure decompensation at a 30-day follow up. Delta weight change, length of hospital stay, and all cause mortality at 90 days	Continuous infusion of furosemide in addition to low-dose dopamine is safe, effective and less nephrotoxic than intermittent boluses. It has a shorter hospital stay and lower readmission rates at 30 days
Amer et al[13]	564	Meta-analysis	Continuous infusion vs. intermittent bolus	24 h	Urine output, reduction in total body weight	Continuous infusion for greater diuresis and reduction in total body weight in patients hospitalized with ADHF

continuous infusion of intravenous furosemide + intravenous dopamine vs. intravenous furosemide bolus in two divided doses vs. intravenous furosemide continuous infusion alone.[14] Their primary endpoint was a negative fluid balance at 24 h after admission. Secondary end points were duration of hospital stay, negative fluid balance at 48, 72,96 h, the trend of serum electrolytes, and renal function and 30 day clinical outcome (death and emergency department visits). Overall, ninety patients were included in the study. There was a greater diuresis in the first 24 h and a shorter hospital stay with the bolus group. There was no significant difference in renal function and serum sodium and serum potassium levels. There was no difference in the number of emergency department visits among the three groups.

They concluded that all three modes of diuretic therapies can be practiced with no difference in worsening of renal function and electrolyte levels. Bolus dose administration with its rapid volume loss and shorter hospital stay might be a more effective diuretic strategy in a resource limited setting of ours, one wishes that they performed the study on greater number of patients. The impact of different strategies on BNP could have been studied.

It is obvious from the above studies that there is no clear consensus on how to administer diuretics during ADHF. One has to use one' own experience, individual patient's clinical status, degree of fluid overload, baseline renal parameters, electrolyte status and also monitor closely BNP, serum creatinine and electrolytes during treatment.

The standard justification for the use of continuous infusion of loop diuretics is to avoid the so called "diuretic resistance". Actually, there is no properly described term as "diuretic resistance". It is used when the patients are unable to meet their clinically required decongestive targets despite large doses of loop diuretics.[15] The pharmacokinetic and pharmacodynamic causes of diuretic resistance are delayed absorption of the diuretic, reduced secretion of the diuretic into the tubular lumen (its site of action), compensatory retention of sodium after the effective period of the diuretic and hypertrophy and hyperplasia of epithelial cells of the distal convoluted tubule.[16] Also drug resistance develops frequently with repeated administration of loop diuretics and, as a consequence, fluid retention and congestion recur. Loop diuretic resistance is likely to be due to the operation of several counter-regulatory processes, including renin angiotensin system (RAAS) which cause fluid retention.[2]

Apart from a continuous infusion of a loop diuretic, the diuretic resistance can be overcome by increasing doses of loop diuretics, use of more potent diuretics like Bumetanide, Torsemide; or a combination of diuretics from different classes such as metolazone or thiazide diuretics.[16]

Combining loop and thiazide diuretics in patients with CHF and diuretic resistance is a very elegant and logical treatment option because it takes into account the pathophysiological mechanism.[15,16]

The indiscriminate use of diuretics not only carries the risk of over-diuresis referred above, but is also related to detrimental effects on renal function, particularly among elderly patients. Even without over-diuresis, high doses of diuretics with concomitant worsening renal function have been tied to both longer hospital length of stay and increased mortality after discharge.[15]

Every intensive care unit should have its own protocol regarding the use of diuretic therapy designed in consultation with intensivist, Cardiologist and Nephrologist and based on the evidence available in the literature. This strategy will prevent overdosing the patients with diuretics.

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