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Case Report

Does Albumin Infusion Improve Loop Diuretic Efficacy and Reduce Third Spacing in Patients Treated for Acute Heart Failure? Case Series and Literature Review

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Abstract

Background: It is well known that hypo-albuminemic patients with nephrotic syndrome are refractory to diuretic therapy. Albumin has been shown to have a direct effect on the efficacy of loop diuretics.

Case series: Four patients admitted for acute de compensated heart failure refractory to outpatient loop diuretic therapy were treated at a tertiary care center. Patient's baseline demographics at admission were similar with respect to diabetes, hypertension, and chronic kidney disease. All patients were on maximum tolerated guideline directed medical therapy for heart failure with reduced ejection. Average New York Heart Association (NYHA) class on admission was 2.8 and decreased to 2.0. Median baseline body weight was 88.4 kg (IQR 25,75 was 83.8 and 91.8, range 82.4-92.9) on admission and 85.0 kg (IQR 25, 75 was 80.0 and 90.3, range 79.6-92.1) at discharge. Baseline median creatinine on admission was 1.69 mg/dl (IQR 25, 75 was 1.58 and 2.25, range 1.54-2.40) compared to median discharge creatinine of 1.59 mg/dl (IQR 25, 75 was 1.36 and 2.28, range 1.29-2.49). The median length of stay was 4.9 days (IQR 25, 75 was 2.75 and 8.175, range 2.1-9.2) and median intensive care unit length of stay was 4 days (IQR 25, 75 was 3.25 and 4.75, range 3-5). The 30 day readmission rate for acute heart failure was 25% of total patients.

Summary: Albumin infusion in addition to parental loop diuretics in these four acute heart failure patients showed improved diuresis and return to dry. The findings from this case series suggest improved loop diuretic efficacy with co-administration of albumin with possible reduction in length of intensive care unit stay and thirty day readmission rate with mechanism of action secondary to increase in plasma on cotic pressure and increased diuretic delivery to the nephron.

Key Words: Albumin infusion; Acute Heart Failure; Loop Diuretics

Introduction

Loop diuretics are commonly used in the treatment of de compensated heart failure, nephrotic syndrome and cirrhotic patients. It is known that hypo-albuminemic patients with nephrotic syndrome do not respond as well to loop diuretics. The mechanism of action of loop diuretics involves inhibition of the sodium potassium chloride transporter in the loop of Henle. Hypoalbuminemia results in decreased diffusion of the diuretic to the extracellular space and causes a reduced amount of the diuretic to reach renal secretary sites [1]. Human albumin represents 50% of proteins within the intravascular circulation and is responsible for 70% of the plasma oncotic pressure [2]. Loop diuretics and other diuretic agents are organic acids which strongly bind to plasma protein primarily albumin [3,5]. In this case series, we report our observations on intensive care unit (ICU) length of stay (LOS) and thirty day hospital readmission rate in a cohort of hypo albuminemic patients undergoing treatment for acute heart failure with co-administration of albumin infusion and loop diuretics.

Case Series

We present 4 cases, all presenting to our facility within two weeks' time, with symptoms of acute heart failure refractory to outpatient loop diuretic therapy. In this group of patients, we utilized albumin infusion prior to initiation of parenteral loop diuretics. The albumin infusion consisted of 25% albumin at 50 ml per hour over a five-hour period of time on average. The albumin was infused for at least one hour prior to the initiation of parenteral loop diuretic treatment, either via continuous infusion or bolus dosing. Baseline data were collected on the patients to include ethnicity and comorbidities to include hypertension, diabetes and chronic kidney disease. The patient's albumin, creatinine, GFR, sodium and hemoglobin were compared on admission compared to that at discharge. The admission body weight was compared to discharge body weight. The electronic medical record (EMR) was queried to determine total diuretic dose administered during the hospitalization. All diuretic doses were converted to oral furosemide equivalent doses using the conversion: bumetanide 1mg=torsemide 20mg=furosemide 40mg. The amount of 25% albumin administered during the hospitalization was also abstracted. The endpoints of interest were ICU LOS, hospital LOS, and 30 day readmission rate.

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Results

The average patient age was 77 years old. Two of patients were Caucasian and 2 were African American. Three patients had type 2 diabetes (DM2) and chronic kidney disease (CKD) and 2 patients had hypertension. All patients were on ace inhibitors, beta blockers and oral diuretics prior to admission. The average ejection fraction of this cohort of patients was 31% and average New York Heart Association (NYHA) class on admission was 2.75, which improved to an average of NYHA class 2.0 at discharge. Median baseline body weight was 88.4 kg (IQR 25,75 was 83.8 and 91.8, range 82.4-92.9) on admission and 85.0 kg (IQR 25, 75 was 80.0 and 90.3, range 79.6-92.1) at discharge with improvement of renal function. Baseline median creatinine on admission was 1.69 mg/dl (IQR 25, 75 was 1.58 and 2.25, range 1.54-2.40) compared to median discharge creatinine of 1.59 mg/dl(IQR 25, 75 was 1.36 and 2.28, range 1.29-2.49). The patients median albumin level was 3.75 g/dl on admission and 3.65 g/dl at discharge The median LOS was 4.9 days (IQR 25, 75 was 2.75 and 8.175, range 2.1-9.2) and median ICULOS was 4 days (IQR 25, 75 was 3.25 and 4.75, range 3-5). The 30 day readmission rate for acute heart failure was 25% of total patients.

Discussion

The data collected on this small cohort of patients admitted with acute heart failure with and reduced ejection fraction who were refractory outpatient oral diuretics showed reduction in body weight suggestive of adequate diuresis with treatment of albumin in addition to intravenous loop diuretics. There was improvement in renal function noted and median albumin levels decreased during the hospitalization. In addition, only 1 patient was readmitted for heart failure at 30 days.

There is limited data upon review of the available literature addressing the potential benefits of albumin infusion to assist diuresis in hypo albuminemic patients being treated for acute heart failure. Inoue et al showed that furosemide resistance was related to hypo-albuminemia in rats. Improved diuresis was observed in an albuminemic rats treated with furosemide bound to albumin [4]. In a small study of 9 patients with nephrotic syndrome, it was noted that the co-administration of albumin modestly improved the effect of furosemide [5].

Hypertonic saline co-administration in small volumes was been observed to improve in patients treated for class IV heart failure [6]. Licata et al randomized 107 patients to treatment with high-dose furosemide with and without small-volume hypertonic saline administration. There was a more significant diuresis in the group who received small-volume hypertonic saline solution infusion compared to control group. These authors postulated that hypertonic saline solution improved diuresis due to an increased osmotic pressure gradient resulting in improved extracellular fluid mobilization into the intravascular space [6].

Other authors have found no effect on patients treated with albumin in addition to loop diuretics for treatment of refractory diuresis. Doungngern et al. retrospectively reviewed 31 total patients admitted to the medical ICU who were treated with continuous infusion of furosemide with about half treated with a continuous six hour infusion of 25% albumin. Patients were monitored for urine output and net fluid loss. There was no statistical difference in diuresis in patients treated with a 6 hour continuous infusion of 25% albumin in addition to continuous intravenous furosemide compared with intravenous furosemide only. The primary underlying illness in this cohort of patients studied was cancer with cardiovascular disease representing only 23% of the total patient cohort [7]. A review article published by Elwell et al. summarized a series of prior studies evaluating the usefulness of furosemide and human albumin for treatment of diuretic resistant edema in patients with nephrotic syndrome and cirrhosis [8]. They concluded the current data was insufficient to make firm conclusions regarding the efficacy of albumin in the treatment of diuretic resistant edema, but it does appear to benefit a select group of patients [8].

Our study is limited by the retrospective, descriptive nature of the data in a small population of patients, and thus is only hypothesis generating. Further prospective, randomized studies will need to be performed to better delineate the utility of co-administration of albumin in acute heart failure and hypo albuminemia.

Conclusion

This case series highlights the opportunity for further research in the form of the development of a randomized controlled trial to further elucidate whether diuretic refractory patients admitted with de compensated heart failure may benefit from albumin infusion to facilitate diuresis.

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