The Efficacy of Furosemide, Salt Tablets, and Fluid Restriction for Treatment of Patients with Syndrome of Inappropriate Antidiuresis: An Open-Label, Randomized, Controlled Study (Effuse-fluid Trial)

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Background: Hyponatremia is associated with increased morbidity and mortality. Syndrome of inappropriate antidiuresis (SIAD) is the most frequent cause of hyponatremia in a hospital setting. First-line therapy for SIAD is fluid restriction, but it is difficult to adhere and may not be effective enough to treat severe hyponatremia.

Objective: This study aimed to investigate whether furosemide in combination with sodium chloride (NaCl) supplement could be more effective than fluid restriction alone in treatment of SIAD.

Methods: A single center, open-label, randomized, controlled study was conducted. Patients with hyponatremia (serum Na <130 mmol/L) due to SIAD were randomly assigned to one of the following groups: 1) fluid restriction alone (FR, n=32), 2) fluid restriction and furosemide (FR+FM, n=30), and 3) fluid restriction, furosemide, and NaCl tablets (FR+FM+NaCl, n=31). Daily fluid restrictions were <0.5 L or <1 L depending on free-water clearance. Furosemide dosage was 20-40 mg once daily and NaCl supplement was 3 gm daily. All treatments were continued until 28 days. The primary end point was serum Na level on day 4 after randomization. The secondary end points were serum Na on day 7 and day 28 after randomization, percentage of patients achieving serum Na of ≥130 or ≥135 mmol/L at day 4 after randomization, and time to achieve serum Na of ≥130 mmol/L.

Results: As shown in the Figure, baseline serum Na levels were not different between the three groups. Mean serum Na levels on day 4 and day 28 were not different in those groups. However, on day 7, mean serum Na level was higher in the FR+FM+NaCl group when compared to the other two groups. The percentage of patients who achieved serum Na of ≥130 and ≥135 mmol/L at day 4 were not different between those three groups (p=0.403 and p=0.645). Time to achieve serum Na of ≥130 mmol/L was also not different between the groups (p=0.141). Notably, time to achieve serum Na of ≥135 mmol/L were longer in the FR group when compared to those in the FR+FSM+NaCl and the FR+FSM groups (18±10 vs 8±7 vs 9±8 days, respectively, p=0.003). The adverse events were not different between those groups.

Conclusion: In hyponatremic patients secondary to SIAD, treatment with furosemide and/or NaCl tablets in combination with fluid restriction are not more effective than treatment with fluid restriction alone. However, the time to achieve serum Na of ≥135 mmol/L is shorter if furosemide and/or NaCl tablets are prescribed.

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