- AJKS March 2020
- First Randomized Control Trial for treatment of SIADH
- Three arms
  - Fluid restriction
  - Na tablets
  - Na+Lasix
- 92 patients, single center, poor adherence to fluid restriction

Efficacy of Furosemide, Oral Sodium Chloride, and Fluid Restriction for Treatment of Syndrome of Inappropriate Antidiuresis (SIAD): An Open-label Randomized Controlled Study (The EFFUSE-FLUID Trial)

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Rationale & Objective: First-line therapy for syndrome of inappropriate antidiuresis (SIAD) is fluid restriction. Additional treatment for patients who do not respond to fluid restriction are water restriction with furosemide or water restriction with furosemide and salt supplementation. However, the efficacy of these treatments has never been tested in a randomized controlled study. The objective of this study was to investigate whether, combined with fluid restriction, furosemide with or without sodium chloride (NaCl) supplementation was more effective than fluid restriction alone in the treatment of hyponatremia in SIAD.

Study Design: Open-label randomized controlled study.

Setting & Participants: Patients with serum sodium concentrations ($[Na^+]$) ≤ 130 mmol/L due to SIAD.

Intervention(s): Random assignment to 1 of 3 groups: fluid restriction alone (FR), fluid restriction and furosemide (FR+FM), or fluid restriction, furosemide, and NaCl (FR+FM+NaCl). Strictness of fluid restriction (<1,000 or <500 mL/d) was guided by the urine to serum electrolyte ratio. Furosemide dosage was 20 to 40 mg/d. NaCl supplements were 3 g/d. All treatments were continued for 28 days.

Outcomes: The primary outcome was change in $[Na^+]$ at days 4, 7, 14, and 28 after randomization.

Results: 92 patients were recruited (FR, n = 31; FR+FM, n = 30; FR+FM+NaCl, n = 31). Baseline $[Na^+]$ was 125 ± 4 mmol/L, and there were no significant differences between groups. Mean $[Na^+]$ on day 4 in all treatment groups was significantly increased from baseline by 5 mmol/L ($P < 0.001$); however, the change in $[Na^+]$ was not significantly different across groups ($P = 0.7$). There was no significant difference in percentage of patients or time to reach $[Na^+]$ ≥ 130 or ≥135 mmol/L across the 3 groups. Acute kidney injury and hypokalemia (potassium ≤ 3.0 mmol/L) were more common in patients receiving furosemide.

Limitations: Open-label treatment.

Conclusions: In patients with SIAD, furosemide with NaCl supplement in combination with fluid restriction did not show benefits in correction of $[Na^+]$ compared with treatment with fluid restriction alone. Incidences of acute kidney injury and hypokalemia were increased in patients receiving furosemide.

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Trial Registration: Registered at the Thai Clinical Trial Registry with study number TCTR20170629004.

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