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## Original Investigation

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# Correction Rates and Clinical Outcomes in Hospitalized Adults With Severe Hyponatremia A Systematic Review and Meta-Analysis

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## Key Points

**Question** For hospitalized adults with severe hyponatremia, what is the association of sodium correction rate with mortality?

**Findings** In this systematic review and meta-analysis involving 16 studies and 11 811 patients, moderate-certainty evidence showed that rapid correction of severe hyponatremia was associated with 32 and 221 fewer in-hospital deaths per 1000 treated patients compared with slow and very slow correction, respectively. Low-certainty evidence suggested that rapid correction was associated with 61 and 134 fewer deaths per 1000 treated patients at 30 days compared with slow and very slow correction, respectively.

**Meaning** The available evidence suggests that slow correction of severe hyponatremia was associated with an increased risk of mortality.

## Abstract

**Importance** Hyponatremia treatment guidelines recommend limiting the correction of severe hyponatremia during the first 24 hours to prevent osmotic demyelination syndrome (ODS). Recent evidence suggests that slower rates of correction are associated with increased mortality.

**Objective** To evaluate the association of sodium correction rates with mortality among hospitalized adults with severe hyponatremia.

**Data Sources** We searched MEDLINE, Embase, the Cochrane Library, LILACS, Web of Science, CINAHL, and international congress proceedings for studies published between January 2013 and October 2023.

**Study Selection** Comparative studies assessing rapid ( $\geq 8\text{-}10 \text{ mEq/L}$  per 24 hours) vs slow ( $<8$  or  $6\text{-}10 \text{ mEq/L}$  per 24 hours) and very slow ( $<4\text{-}6 \text{ mEq/L}$  per 24 hours) correction of severe hyponatremia (serum sodium  $<120 \text{ mEq/L}$  or  $<125 \text{ mEq/L}$  plus severe symptoms) in hospitalized patients.

**Data Extraction and Synthesis** Pairs of reviewers (N.A.F., J.R.M., J.M.A., A.C.) independently reviewed studies, extracted data, and assessed each included study's risk of bias using ROBINS-I, Cochrane methods, PRISMA reporting guidelines, and the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to rate the certainty of evidence were followed. Data were pooled using a random-effects model.

**Main Outcomes and Measures** Primary outcomes were in-hospital and 30-day mortality, and secondary outcomes were hospital length of stay (LOS) and ODS.

**Results** Sixteen cohort studies involving a total of 11 811 patients with severe hyponatremia were included (mean [SD] age, 68.22 [6.88] years; 56.7% female across 15 studies reporting sex). Moderate-certainty evidence showed that rapid correction was associated with 32 (odds ratio, 0.67; 95% CI, 0.55-0.82) and 221 (odds ratio, 0.29; 95% CI, 0.11-0.79) fewer in-hospital deaths per 1000 treated patients compared with slow and very slow correction, respectively. Low-certainty evidence suggested that rapid correction was associated with 61 (risk ratio, 0.55; 95% CI, 0.45-0.67) and 134 (risk ratio, 0.35; 95% CI, 0.28-0.44) fewer deaths per 1000 treated patients at 30 days and with a reduction in LOS of 1.20 (95% CI, 0.51-1.89) and 3.09 (95% CI, 1.21-4.94) days, compared with slow and very slow correction, respectively. Rapid correction was not associated with a statistically significant increased risk of ODS.

**Conclusions and Relevance** In this systematic review and meta-analysis, slow correction and very slow correction of severe hyponatremia were associated with an increased risk of mortality and hospital LOS compared to rapid correction.

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