

Evaluation of the Relationship Between Fractures and Hyponatremia

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Purpose: Hyponatremia is frequently present in the elderly population. Recent studies show an increased risk of fractures in patients with mild chronic hyponatremia. Hyponatremia upregulates osteoclast-mediated bone resorption. Our study evaluates the relationship between hyponatremia and risk of incident fracture while controlling for bone density, age, and sex.

Methods: A retrospective, matched case-controlled study was performed. Patients ≥ 45 years old with dual-energy x-ray absorptiometry (DEXA) scans and serum sodium obtained within a year prior to event of interest (fracture/nonfracture complaint) were included. Cases were defined as patients with an incident fracture (vertebra, femur/hip, tibia/fibula, and forearm) between January 2005 and May 2013. The first fracture was used for cases with multiple fractures. Controls were defined as patients with a nonfracture complaint over the same time period, matched 2:1 with cases on age (within 2 years) and sex. Data on disease modifiers including medications and disease conditions that could influence sodium levels and osteoporosis risk were also obtained. Hyponatremia was defined as: absent (>137 mmol/L), low-normal (135-137 mmol/L), mild (130-134 mmol/L), or moderate-severe (<130 mmol/L). Bone density classification was defined as: osteopenia = T-score -1.0 to -2.5 , and osteoporosis = T-score <-2.5 ; univariate and multivariate conditional logistic regression models were used to estimate risk of fracture with hyponatremia and bone density. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. All statistical analysis was performed using SAS v9.3. All tests were two-sided with $\alpha = 0.05$.

Results: We identified 457 cases and 914 controls. Mean age was 73 ± 10 years old and 89% females. Hyponatremia was more prevalent in cases compared to the controls. Univariate logistic regression models showed a significantly higher risk of fracture in hyponatremia ($P < 0.0001$) and osteoporosis/osteopenia ($P < 0.0001$). Vertebral fractures were associated with worsening hyponatremia, compared to nonvertebral fractures (χ^2 , $P = 0.0002$). A similar pattern was observed in femur fractures when compared to other nonvertebral fractures (χ^2 , $P = 0.04$). On multivariate analysis, controlling for presence of known disease modifiers, the risk was 3-fold higher in mild (OR 3.0; 95% CI: 2.2, 4.2), 4-fold higher in moderate (OR 4.4; 95% CI: 2.8, 7.0) and 11-fold higher in severe hyponatremia (OR 11.1; 95% CI: 4.1, 30.5). A reverse trend was seen among patients with forearm and tibia/fibula fractures who tended to be younger.

Conclusion: Our study shows an increased risk of fractures in patients with varying degrees of hyponatremia irrespective of radiologic bone density changes. In addition the risk of fracture appeared to increase with worsening hyponatremia while controlling for known disease modifiers. This highlights the importance of recognizing and managing hyponatremia and its associated morbidity including fractures.

See pages 99 - 147 for financial disclosure information.