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New approach to hyponatremia yields high prevalence and identification of natriuretic protein that causes renal salt wasting and new syndrome of renal salt wasting in Alzheimer's disease.

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The approach to hyponatremia is in a state of flux, especially in differentiating syndrome of inappropriate secretion of antidiuretic hormone (SIADH) from cerebralrenal salt wasting (RSW) because of diametrically opposite therapeutic goals of water-restricting in SIADH and administering saline in RSW. We differentiated SIADH from RSW by utilizing an algorithm based on fractional excretion (FE) of urate and failure of isotonic saline infusions to dilute the urine or correct the hyponatremia in SIADH as compared to excretion of dilute urines and correction of hyponatremia in RSW. We also identified the natriuretic factor we previously demonstrated in neurosurgical patients with RSW and in Alzheimer's disease (AD).

Results: Of 62 hyponatremic patients, (A) 17 patients (27%) had SIADH, 11 were nonresponsive to isotonic saline, and 5 normalized a previously high FEurate after correction of hyponatremia; (B) 19 patients (31%) had a reset osmostat based on normal FEurates and spontaneously excreted dilute urines; (C) 24 patients (38%) had RSW, 21 had no clinical evidence of cerebral disease, 19 had saline-induced dilute urines; 2, 10 required D5W to prevent rapid increases in serum sodium to prevent osmotic demyelination, 11 had persistently increased FEurate after correction of hyponatremia. (D) 1 patient had Addison disease with a low FEurate and (E) 1 patient (1.6%) had hyponatremia due to hydrochlorothiazide. We identified haptoglobin related protein without signal peptide (HPRWSP), the first potent inhibitor of proximal tubule sodium transport, as the natriuretic factor in a patient with RSW and in AD.

Conclusions: RSW is much more common than is perceived with 21 of the 24 patients with RSW lacking evidence of cerebral disease, supporting our proposal to change cerebral salt wasting to RSW. HPRWSP can serve as a biomarker for RSW to simplify diagnosis of RSW on first encounter, direct proper therapy, improve clinical outcomes and identifying a new syndrome of RSW in AD. HPRWSP will more effectively treat congestive heart failure when combined with a distal diuretic.

Biography

John Maesaka is presently professor of medicine at the NYU Long Island School of Medicine and Chief Emeritus of the Division of Nephrology and Hypertension at the NYU Langone Hospital Long Island. He was born in Hawaii, received a BA degree from Harvard University, an MD degree from the Boston University School of Medicine and trained at Barnes Jewish Hospital at Washington University in St. Louis and the Mount Sinai Hospital and Medical School in New York. He also spent 5 years exclusively in the physiology laboratory at Mount Sinai Medical Center, which prepared him well for his future research endeavors. He has spent many years studying hyponatremic conditions, especially renal salt wasting and identifying the protein that causes it.