Hyponatremia in the Intensive Care Unit

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Summary: Hyponatremia is a common electrolyte disturbance encountered in the intensive care unit setting. The underlying etiology is multifactorial and includes processes that lead to both a baroreceptor-mediated and a baroreceptor independent increase in antidiuretic hormone release. Patients with hyponatremia have an increased mortality rate and therefore an understanding of the cause and treatment of this disorder is of paramount importance.
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Hyponatremia is a common electrolyte derangement in hospitalized patients and is associated with increased mortality. The mortality rate in hyponatremic patients is approximately 3 times that of normonatremic hospitalized patients.[1,2] Outcomes are particular poor in those patients whose serum sodium level decreases during a hospitalization. In a recent retrospective cohort study of 10,899 hospitalized patients the incidence of hyponatremia (serum sodium level, <135 mmol/L) at admission was 5.5%.[3] As compared with those with a normal serum sodium, these patients were more likely to require intensive care and mechanical ventilation within 48 hours of hospitalization. In addition, hospital mortality, mean length of stay, and costs were significantly greater among patients with hyponatremia than those without.

The association with hyponatremia and adverse outcomes could be the direct result of hyponatremia, the comorbidities that lead to the electrolyte derangement, or both. Whatever the mechanism, hyponatremia should not be viewed as an innocuous condition. Rather, clinicians should view this disorder with urgency and institute measures to prevent any further decline in the serum sodium concentration and initiate appropriate therapy for its correction. This review briefly summarizes the pathogenesis of hyponatremia and then discusses various disease states encountered in the intensive care unit in which hyponatremia frequently is present.

PATHOGENESIS OF HYPONATREMIA

Hyponatremia generally is associated with a hypo-osmolar state and is a marker for a disturbance in water balance. Stated differently, all hyponatremia is dilutional. The presence of hypotonic hyponatremia implies that water intake exceeds the ability of the kidney to excrete water. In unusual circumstances, this can occur when the kidney's ability to excrete free water is intact. However, because a normal kidney can excrete 20 to 30 L of water per day, the presence of hyponatremia with normal renal water excretion implies that the patient is drinking more than 20 to 30 L water per day. This condition is referred to as *primary polydipsia*. Although primary polydipsia is a common condition that leads to polyuria and polydipsia, it is uncommon as a sole cause of hyponatremia.

In the absence of primary polydipsia, hyponatremia is associated with decreased renal water excretion and urine that is concentrated inappropriately. It is important to note that in the presence of hyponatremia urine should be maximally dilute and a urine osmolality higher than this 100 mOsm/L is inappropriate. A number of clinical conditions lead to hyponatremia by limiting renal free water excretion. These

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conditions generally can be divided according to the extracellular fluid volume.

Conditions that lead to a decreased effective arterial volume will cause increases in arginine vasopressin (AVP) levels and decreases in distal delivery of filtrate, both of which will limit free water excretion and lead to increases in urine osmolality. In addition, a decreased effective arterial volume will increase thirst. These specific conditions can be divided into those in which total extracellular volume is decreased, such as diuretics, osmotic diuresis, mineralocorticoid deficiency, salt-losing nephropathy, vomiting, and diarrhea; and into edematous conditions such as congestive heart failure, cirrhosis, nephrosis, and third-space volume losses. In the latter conditions extracellular fluid volume is increased and effective arterial volume is decreased. From the standpoint of AVP regulation and renal regulation, the body responds to effective arterial volume and does not seem to recognize the state of the extracellular fluid volume.

In a number of conditions, hyponatremia is associated with a normal volume state. In these conditions effective arterial volume is normal and increased levels of AVP cannot be attributed to decreases in effective arterial volume or to increases in tonicity. These conditions include the syndrome of inappropriate antidiuretic hormone secretion (SIADH), glucocorticoid deficiency, hypothyroidism, drugs, and stress.

CLINICAL CONDITIONS ASSOCIATED WITH HYPONATREMIA IN THE INTENSIVE CARE UNIT

Postoperative Hyponatremia

The postoperative patient is particularly prone to develop hyponatremia. AVP levels are increased for several days after surgical procedures because of baroreceptor- and nonbaroreceptor-mediated mechanisms. These patients typically have subtle or overt decreases in effective arterial blood volume owing to prolonged preoperative fasting combined with intraoperative and postoperative blood loss and third spacing of fluid. In addition to these factors that unload baroreceptors, postoperative pain, stress, anxiety, nausea, and administration of morphine can further stimulate the release of AVP. In some instances nonsteroidal anti-inflammatory drugs are given, which have the effect of augmenting the hydro-osmotic actions of AVP.[4] In this setting of compromised ability to excrete a water load, administration of hypotonic fluid can precipitate acute iatrogenic hyponatremia.

Postoperative hyponatremia has been a major problem in pediatric populations because to the widespread practice of using hypotonic fluids for maintenance therapy. This approach is based on guidelines developed 50 years ago based on calculations linking energy expenditures to water and electrolyte losses.[5] More recently, several groups have argued that isotonic rather than hypotonic fluids should be the routine maintenance fluid in such patients.[6,7] The pediatric community has been slow to embrace this approach out of the concern that excessive administration of sodium would increase the risk of hypernatremia. A systematic meta-analysis of studies comparing isotonic and hypotonic fluids in hospitalized children found the odds of developing hyponatremia after hypotonic solutions was 17.2 times greater than with isotonic fluids.[8] The concern that isotonic maintenance fluids carry a risk of hypernatremia was not supported in the review. Some studies actually reported a decrease in serum sodium concentration, presumably as a result of the desalination phenomenon in which hypertonic urine is excreted in the urine in volume-expanded subjects with persistent vasopressin secretion.

Endocrine Disorders

Glucocorticoid Deficiency

Patients with glucocorticoid deficiency develop hyponatremia. It is important to separate this condition from that of mineralocorticoid deficiency and combined mineralocorticoid-glucocorticoid deficiency. In patients with mineralocorticoid deficiency, extracellular fluid volume and effective arterial volume are low. This leads to baroreceptor stimulation of vasopressin secretion and to decreased distal delivery of filtrate to the diluting segments of