Journal of Internal Medicine and Emergency Research

ISSN: 2582-7367
Ahmad N, et al., 2023-Intern Med Emerg Res
Review Article

Management of Low Sodium in AMU

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Received Date: 10-02-2023

Accepted Date: 10-12-2023

Published Date: 10-24-2023

Abstract

Hyponatremia is a common finding in acutely ill patients and is defined as serum sodium (Na) level less than 135 mEq/L which is due to a relative excess of water in relation to serum sodium. Reasons for hyponatremia are increase in water intake (hypotonic intravenous fluid therapy or primary polydipsia) or impaired water excretion due to renal failure or increase release of antidiuretic hormone. Optimum management depends on the duration and severity of hyponatremia and involves close monitoring and accurate fluid balance assessment.

We will discuss in this article the basics of management, pitfalls to avoid in Hyponatremia and recommended approach based on literature review when reviewing a patient with Hyponatremia, firstly to enquire about the duration of Hyponatremia to differentiate acute from chronic as the threshold for treatment is different, following duration is assessment of severity (clinically by symptoms and signs as well as biochemistry) as severity will affect the management. Following duration and severity the acute physician should assess the volume status of the patient to hypovolemic, euvolemic or hypervolemic Hyponatremia which aids in reaching the possible cause of Hyponatremia and the right treatment.

Keywords: Hyponatremia; SIADH; Hypertonic saline; Cerebral oedema; Osmotic demyelination syndrome.

Introduction

Assessment of volume status starts by history taking and clinical examination signs

Indicators of hypovolemia (reduced oral intake, vomiting, diarrhea, drugs like diuretics) and signs of fluid depletion (postural hypotension, tachycardia with low blood pressure or delayed capillary refill time with cold peripheries).

Indicators of hypervolemia and signs of fluid overload (raised engorged jugular venous pressure (JVP), hypertension with dependent oedema).

Biochemistry is important in aiding diagnosis but usually results can take 24 hours or more and the usual approach is to arrange for renal profile, thyroid function, random or 9 am cortisol and send urine for cations and osmolality paired with serum osmolality.

Normal serum osmolality is 280-295 mOsm/Kg and in a context of Hyponatremia can points towards raised protein or hyperlipidemia, raised serum osmolality can occur in presence of hyperglycemia or high osmolality agents like mannitol, while low serum osmolarity Hyponatremia is the most common finding which confirms true Hyponatremia.

Urine osmolality below 100 mOsm/Kg in the presence of Hyponatremia is a normal physiology which suggests a suppressed antidiuretic hormone (ADH) with full water excretion capacity which can occur in psychogenic polydipsia or autocorrection after treating any cause of Hyponatremia, while higher levels over 150 mOsm/Kg points towards impaired water excretion due to ADH which occurs in syndrome of inappropriate ADH (SIADH) or any cause of poor renal perfusion (hypovolemia or hypervolemia).

Fractional excretion of sodium (FENa) is more accurate than urinary sodium, in Hyponatremia with normal renal function FENa below 1% points towards hypovolemia while FENa over 1% points towards normovolemia or hypervolemia [1].

Often differentiating between hypovolemic Hyponatremia and SIADH can be tricky and not straight forward, clues for SIADH are euvolemic status without postural hypotension, normal renal, thyroid, and adrenal function, urine osmolarity more than 100 mOsm/Kg, urinary Na more than 40 mmol/L in presence of normal salt in diet and absence of diuretic use within the last week, FENa more than 1%, and low uric acid below 237 mmol/L [1]. If uncertainty between hypovolemic Hyponatremia and SIADH persists, and urinary tests are delayed or not available a trial of isotonic saline can differentiate between hypovolemia and SIADH where the serum Na improves in the former while it doesn't or even lowers further in SIADH [1].

Discussion

The treating physician who is dealing with a case of Hyponatremia requires to know the answer for three questions to be able to manage the case adequately:

First question is the duration of hyponatremia

While acute Hyponatremia occurs within 48 hours, chronic occurs more than 48 hours, the threshold for treatment is much lower in acute Hyponatremia due to the higher risk for deterioration and serious complications compared to chronic Hyponatremia, chronic Hyponatremia of more than 48 hours requires less aggressive management as overcorrection can cause serious complications due to brain adaptation which did not occur yet in acute cases.

Second question to be answered is the severity of hyponatremia

Severe is defined as serum Na below 120 mEq/L and carries a high risk of morbidity and mortality if not treated adequately or

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DOI: https://doi.org/10.37191/Mapsci-2582-7367-4(3)-065

indeed over treated aggressively, mild Hyponatremia is serum Na of 130-134 mEq/L and is usually asymptomatic, and moderate Hyponatremia which is classified as serum Na of 120-129 mEq/L and can cause symptoms like nausea, vomiting, headache, and falls due to dizziness and gait disturbance. Clinical presentation of patients with Hyponatremia can vary from asymptomatic to life-threatening, usually symptoms are coinciding with biochemistry and severe symptoms like delirium, coma, seizures, and respiratory arrest can occur in acutely severe Hyponatremia below 120 mEq/L due to rapid fluid shift without enough time for the brain to adapt leading to cerebral oedema, brainstem herniation and death if not treated early.

Chronic Hyponatremia on the other hand, has time for brain adaptation, so levels of Na below 110 mEq/L presents less frequently with life-threatening features compared to same levels in acute Hyponatremia [2].

In moderate acute Hyponatremia presenting with even mild symptoms, it is essential to be aware that life-threatening features may occur soon if treatment is not initiated early [3]. Therefore, acute physician should be aware of and monitor closely any patient presenting with acute moderate or severe Hyponatremia and consider early treatment within six hours to minimize cerebral oedema while avoiding over correction which can lead to osmotic demyelination syndrome (ODS [4].

Before answering the third question, when acute physician is confident that he/she is dealing with a case of acute and severe Hyponatremia an urgent action is required before moving on, the Initial target is to treat aiming an increase in serum Na up to 6 mEq/L within six hours and maintain this level in the first 24 hours, even if symptoms did not improve there is no benefit and potential harm by further increase in serum Na levels in the first 24 hours [5].

Over correction of severe Hyponatremia may risk ODS, risk is higher in alcoholics, liver disease, electrolyte deficiency like low potassium and phosphate, and with serum Na below 105 [6].

Overcorrection is common, and it is not advisable to increase serum Na by more than 8 mEq/L in the first 24 hours or 18 mEq/L in the first 48 hours [7].

As mentioned above, patients with symptomatic acute severe Hyponatremia are likely suffering from early cerebral oedema due to increased intracranial pressure and early treatment within six hours with 100 mL of 3% saline over ten minutes or 150 mLs over 20 minutes is indicated, serum Na should be checked after each dose and infusion should be stopped when serum sodium increase by 5-6 mEq/L or maximum of 300 mLs given [8].

Serum Na should be monitored hourly until target is achieved and then less frequently afterwards to ensure overcorrection is not happening. If serum Na level is over corrected with treatment specially in the presence of signs of autocorrection like an increase in urine output which is diluted with specific gravity below 1.005 and osmolality below 200 mOsmol/kg with a reduction in the urine cation (urine Na/K) or urine sodium below 20 there is high risk at this stage for the development of ODS and recommendations

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are to start 1-2 mcg of desmopressin every six to eight hours until the serum Na has not exceeded the target, this approach is preferred than initiating 5% dextrose which can exacerbate thiamine or electrolyte deficiency, further discussion regarding treating overcorrection below [9].

The first part of the discussion focused on diagnosing and managing acute severe or moderate symptomatic Hyponatremia with in the first 6 hours with some advice on monitoring and managing overcorrection, the second part of this discussion will explain the management of Hyponatremia moving forward after ensuring that the risk of cerebral oedema is minimal, and management will depend on the cause of Hyponatremia which requires the acute physician to ask the third and last question, volume status?

Third question is the volume status and fluid assessment

This is essential in managing stable patients with Hyponatremia; however, this assessment can be challenging for many reasons, most difficult scenarios here is managing a patient with intravascular depletion and extravascular volume overload and we recommend a global assessment including history taking, full examination and biochemistry (blood and urine).

Hypervolemic hyponatremia

Requires fluid restriction which is not a fixed amount of oral intake per day but in simple words the aim is to create a negative fluid balance which is oral fluid intake below the total urine output in 24 hours or restricting to 60% or less of the daily fluid requirement (daily fluid requirement is usually 30 mLs/Kg or 25 mLs/kg in frail elderly patients). Creating a negative water balance is the main treatment for patients with fluid overload like in advanced heart, liver, or oliguric renal failure as well as patients with syndrome of inappropriate antidiuretic hormone (SIADH) and psychogenic polydipsia.

Fluid restriction is often not enough in patients with concentrated urine of 500 mOsmol/kg or more and in these circumstances a lower restriction threshold to below 800 mLs of water per day is required to improve Hyponatremia [10].

Furosemide inhibits NaCl reabsorption in the thick ascending limb of loop of Henle and creates an antidiuretic hormone (ADH) resistance status leading to more water than Na loss, furosemide can be used if water restriction is not effective and one way to check if restriction is enough or furosemide is required is by checking urine to serum cation ratio (urine Na+K divided by serum Na) if the ratio is below 0.5 restriction will work and if the ratio is over 1 then furosemide add on is beneficial [11].

Tolvaptan is a V2 vasopressin receptor antagonist which enhance water diuresis without affecting Na or K levels, it is contraindicated in liver cirrhosis and should not be used for more than 30 days, tolvaptan can be used in hypervolemic Hyponatremia or resistant cases of SIADH, when tolvaptan is used fluid restriction should be stopped due the risk of hypotension and renal failure [12].

Oral salt tablets are contraindicated in patients with fluid overload but for SIADH with serum Na over 120 mEq/L or

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hypovolemia oral salt tablets can be given, 1 g of oral salt is equivalent to 35 mL of 3% saline and can be given with fluid restriction in resistant cases of SIADH or with water in mild dehydration [13]. SIADH is characterized by euvolemia with normal renal, thyroid, and adrenal function and biochemistry criteria was mentioned above.

Hypovolemic hyponatremia

Occurs due to intravascular volume depletion leading to excess ADH secretion, administration of isotonic saline aiming for euvolemia will suppress ADH within minutes and restore serum Na levels, important reminder is to avoid overcorrection and when signs of autocorrection like an increase in diluted urine output with specific gravity below 1.005 and osmolality below 200 mOsmol/kg with a reduction in the urine cation (urine Na/K) or urine Na below 20 it is essential here to keep the fluid balance at least neutral as a negative fluid balance can risk ODS due to significant rise of serum Na over the target of 8 mEq/L in the first 24 hours and 18 mEq/L in the first 48 hours [7].

However, if the rise in sodium is quick after the first saline bag, recommendations are to switch isotonic saline to crystalloid with less sodium like Hartmann's or dextrose/saline if serum Na is rising rapidly to avoid the rapid rise in serum Na while maintaining euvolemia, a common Pitfall in treating hypovolemic Hyponatremia is using isotonic saline aggressively. Even in acute severe or symptomatic Hyponatremia, isotonic saline is recommended only for patients with mild to moderate Hyponatremia (serum Na over 120 mEq/L) with no or minimal symptoms, or in patients with significant hypovolemia with postural hypotension, shock, or acute renal failure [14].

When overcorrection occurs on Hartmann's or dextrose saline and serum Na is rising more than 8 mEq/L during treatment in the first 24 hours it is recommended to use 6 mL/kg of dextrose 5% over two hours, this amount is expected to reduce the serum Na by 2 mEq/L roughly and can be repeated to achieve target serum Na, caution in malnourished or alcoholics as risk of thiamine deficiency and electrolyte imbalance. If further concerns regarding very rapid rise of serum Na recommendations are to add desmopressin 1-2 mcg every 6-8 hours to prevent serum Na from rising again [15].

Isotonic saline is contraindicated in hypervolemic Hyponatremia and SIADH, Isotonic saline will worsen fluid overload in the former and will lower the serum Na levels further in patients with SIADH (desalinization). This fact can be useful when facing a difficult case like thiazide induced Hyponatremia which can produce a state of hypovolemia Hyponatremia or SIADH, while waiting for the rest of biochemistry and urine results a trial of one bag of isotonic saline can differentiate between both condition, serum Na will rise, and urine output will increase in case of hypovolemic hyponatremia while serum Na may fall, and urine output will not increase in SIADH [16]. Another concern regarding aggressive use of isotonic saline in hypovolemic Hyponatremia other than a rapid increase in serum Na, is the risk of hyperchloremic metabolic acidosis, one liter of isotonic saline may increase chloride level by 3 mEq/L with multiple use of isotonic saline the chloride level can increase leading to normal anion gap metabolic acidosis, acute

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renal failure due to poor perfusion, and increase risk of mortality in acutely ill patients [17].

Conclusion

The authors suggest a structured approach to patients with Hyponatremia starting by clarifying the duration of Hyponatremia, then assessing the severity (clinically and biochemistry) with initiation of hypertonic saline in acute severe Hyponatremia or acute moderate symptomatic Hyponatremia. Following the duration and severity of the hyponatremia, the acute physician requires to assess volume status through history and clinical examination and finally requests relevant investigations to be able to reach the right diagnosis and the proper management.

Learning points

1. No role for isotonic saline in acutely severe Hyponatremia (serum Na < 120 mEq/L).
2. Hypertonic saline is indicated in acute severe Hyponatremia or acute moderate Hyponatremia with symptoms (vomiting, headache, or confusion).
3. Hypervolemic Hyponatremia is treated by fluid restriction and furosemide.
4. SIADH is treated with fluid restriction and salt tablets.
5. Hypovolemic Hyponatremia is treated with isotonic saline with a low threshold to change to another type of fluid with lower Na content.
6. Serum Na should not rise by more than 8 mEq/L in the first 24 hours or 18 mEq/L in the first 48 hours.
7. Close monitoring of serum Na hourly until target achieved, then less frequently with consideration of dextrose and/or desmopressin if overcorrection occurs.

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