Post-operative orthopaedic hyponatremia: Etiology and clinical approach

Dr. Channareddy H and Dr. Ambrish Sharma

DOI: https://doi.org/10.22271/ortho.2018.v4.i2i.84

Abstract

Hyponatremia is common after orthopaedic surgeries. The prevalence of hyponatremia in the post-operative period is 25-40% in elderly patients. It can cause serious and potentially life threatening complications.

Identifying the cause (etiology) and providing appropriate treatment can mitigate the adverse effects of hyponatremia. Depending on the underlying cause, the treatment of hyponatremia can be markedly different. The aim of the study is to determine the cause of post-operative orthopaedic hyponatremia.

Methods: This is a prospective study of adults aged more than 65 years admitted with major lower limb fractures who developed post-operative hyponatremia. ECF volume status was assessed by clinical examination and biochemical parameters.

Results: Thirty five patients developed post-operative hyponatremia. The most common cause of post-operative orthopaedic hyponatremia was hypovolemia 45.71% (n=16), followed by euvolemia (SIADH) in 25.71% (n=9). Acute kidney injury, hypervolemia and medications each in 3 cases (8.57% each), hypotonic fluids in one case. Etiology was multifactorial in 77.14% (n=27).

Conclusions: Hypovolemia and euvolemia with SIADH are the two major causes of hyponatremia after orthopaedic surgery. The treatment requirements are exact opposites. Hypovolemia requires rehydration with IV fluids where as SIADH needs fluid (free water) restriction. Understanding the etiology of hyponatremia helps to treat hyponatremia with optimal use of IV fluids and avoids adverse outcomes.

Keywords: Orthopedic surgery, post-operative, hyponatremia, causes, diagnosis, practical approach

Introduction

Hyponatremia is a common electrolyte disorder and can lead to neurological complications. Post-operative period represents a significant risk for the development of hyponatremia. The prevalence of hyponatremia during post-operative period is upto 25 to 30%.[1-2]

Hyponatremia is associated with multiple poor clinical outcomes including prolonged hospital stay, increased mortality and morbidity rates.[3]

The underlying cause of hyponatremia may be obvious if a precipitating cause is present such as vomiting, renal failure, blood loss after surgery or any other concurrent illness (risk factors). In most cases the differential diagnosis of hyponatremia is frequently complex and includes a wide range of pathophysiological settings with varying treatment.

Successful treatment of hyponatremia depends upon accurate diagnosis of the underlying etiology of hyponatremia. Identifying the cause of hyponatremia and appropriate treatment can diminish or mitigate the adverse effects of hyponatremia.[4]

The aim of the study is to identify the primary cause of hyponatremia using clinical and biochemical evaluation of patients with hyponatremia who have undergone surgery for major orthopaedic fractures.

Methods

This is a prospective study, conducted at tertiary care hospital and academic institution between 2015 and 2017. Patients more than 65 years old, who have developed post-operative hyponatremia following orthopaedic surgery for major bone fractures of lower limb were included in the study. Exclusion criteria – patients with head injury, patient who were treated conservatively without surgery were excluded.
Hyponatremia is defined as serum sodium measurement of <135 m mol/L. The critical next step is to determine the patients ECF (extra cellular fluid volume) status in the diagnosis of the underlying etiology of hyponatremia. Hyponatremia can be associated with hypovolemia, hypervolemia or euvolemia. ECF status can be assessed with history (vomiting, diarrhea, blood loss after trauma or surgery) fluid input output charts and physical examination. Parameters for clinical assessment of ECF volume status by physical examiantion are given in table No.1 [6]. Clinical examination findings of volume status (hypo/euvolemia/hypervolemia) can be corroborated by laboratory (Bio-chemical) parameters.

Orthostatic Hypotension: > 20 mm decreased in BP and or >20 bpm increased in pulse rate (tachycardia) going from supine to standing position. If the ECF volume status is not certain based on the physical examination, biochemical evaluation should be done to classify volume status [6] (Table No.2). Still any doubt about volume status - Saline infusion test is done and response to therapeutic trial of IV normal saline infusion will reveal the volume status [7].

| Table 1: Clinical evaluation of extra cellular volume (ECF) status: |
|---------------------------------------------------------------|
| **Hypovolemia (Dehydration)** | **Hypervolemia** | **Euvolemia (SIADH)** |
| Dry skin and mucus memberanes(dry tongue) | Peripheral edema in non-surgical extremities or sacral edema | Diagnosed in the absence of any clinical signs of hypovolemia or hypervolemia. |
| Decreased axillary sweating (dry axilla) | Ascitis | SIADH is a diagnosis of exclusion. |
| Decreasedskin turgor | JVP ↑ | Edema-not seen clinically |
| Orthostatic hypotension | CVP ↑ | |
| JVP ↓ | signs of pulmonary edema | |
| CVP ↓ | LVF | |
| Urine output ↓ | | |
| Cognitive impairment | | |
| Weight loss | | |

| Table 2: Heamodynamic and Biochemical measurements: to differentiate ECF volume status6 |
|---------------------------------------------------------------|
| **Haemo concentration** | **Haematocrit (Hct/PCV)** | **S. total proteins** |
| 38-50% (M) | 36-46% (F) | 5.5-8gm/dl |
| **Biochemical** | **Blood urea** | creatinine ratio |
| ↑ (> 80 mg%) | 20-40mg% | ↓ or normal |
| **BUN** | creatinine ratio |
| ↑ (<20) | 10-20 mg% | ↓ (<10 mg/dl) |
| ↓ | (≤3.57 mmol/L) | Normal |
| **S. Uric acid** | | |
| ↑ or normal | M-3.5-7.2 mg% | ↓ (<4mg%) |
| (>5 mg% or | F-2.6-6 mg% | (<0.24 mmol/L) |
| ≥ 0.3 mmol/L) | | ↓ |
| Urinary sodium excretion | <20 mmol/L | >40 mmol/L |

Laboratory parameters to differentiate ECF volume status.

Hypervolemia can be easily detected by clinical examination, but it is difficult to differentiate euvolemia from subtle hypovolemic states [8]. Volume depletion can be diagnosed clinically from the history, physical examination and laboratory results. Patients without signs of volume depletion or volume expansion (subcutaneous edema, ascitis) should be considered to have euvolemia. The underlying cause of hyponatremia is identified based on the findings from history, medications patient is taking, physical examination, laboratory investigation, fluid balance (input and output) charts and evaluation of ECF volume status.

**Results**
Thirty five patients who developed post-operative hyponatremia after major orthopedic fractures between 2015 and 2017 were studied. Patient demographics and clinical characteristics are given in table No.3.
Hypovolemia 45.71% (n=16)

Establishing the etiology of hyponatremia is notoriously challenging and requires accurate assessment of volume status. Hyponatremia can occur when there is either sodium loss or more commonly water retention. Total body water can increase as a result of increased intake or decreased renal clearance. This decreased excretion of water by the kidneys is due to the action of anti diuretic hormone (ADH or AVP) in the post-operative period.

Normally the prime regulator of ADH secretion is plasma osmolality but there is also osmolality independent stimuli – (non-osmotic path way) – is dependent on barroreceptors in the major arterial system. With decrease in cardiac output or hypovolemia (blood loss after surgery) from any cause, non-osmotic pathway is stimulated and it overrides the osmotic pathway and results in release of AVP, activation of RAA–Rennin–Angiotensin–Aldosterone system and norepinephrine release, resulting in water reabsorption from distal renal tubule and collecting ducts of the kidney and water retention.

The non-osmotic stimuli for ADH release includes the stress of surgery, post-operative pain, nausea, hypoxia, hypercarbia, pro-inflammatory cytokines (CRP, interleukins) [9]. Hyponatremia develops as a consequence of increased ADH levels, which can occur in many conditions including trauma, surgery, blood loss, hypovolemia, inappropriate secretion of ADH (SIADH), post-operative states. This is exacerbated by the use of hypotonic fluids and medications (thiazide diuretics, SSRIS etc.) during post-operative period[10]. This peri-operative stress response can last for 12 hours after minor surgery or 4 days after major surgery[11].

The etiology of hyponatremia in elderly patients is predominantly multi factorial [12, 13]. Hypovolemia (dehydration) is a major cause of hyponatremia. This is the simplest and easily treatable cause of hyponatremia. Hypovolemic hyponatremia is accompanied by extra cellular fluid (ECF) volume deficit (depletion). Hypovolemia may due to blood loss from trauma or surgery, decreased oral intake, inadequate replacement of IV fluids and use of diuretics, GI loss – vomiting diarrhea etc. A variety of medications can cause hyponatremia by drug induced SIADH or circulating volume depletion[14].

Euvolemic hyponatremia – there is a relative excess of water compared to sodium. Edema is not seen clinically because the excess water is mainly intra cellular.

SIADH is the most common cause of non-osmotic AVP release in euvolemic hyponatremia. SIADH is a diagnosis of exclusion [15]. SIADH is due to non-osmotic release of ADH. Post-operative state (surgical stimulus-stress, pain, anxiety, nausea, vomiting) coupled with use of hypotonic fluids and medications (narcotics, SSRIS) are prone to develop SIADH.

SIADH must also be considered in patients with pulmonary infections – pneumonia, pulmonary abscess, active TB, asthama, CNS infection, neoplasm (Carcinoma).

Blood urea is highly sensitive to hypovolemia. Increased levels suggest hypovolemia, where as decreased levels indicates euvolemia or hypervolemia (increased ECF volume). In SIADH the ECF volume is expanded so blood urea levels are decreased[16]. Serum uric acid levels are also used in the differential diagnosis of hyponatremia. Serum uric acid levels are increased in hypovolemia and decreased in euvolemia (SIADH) [17]. Algorithm for diagnosis of etiology of hyponatremia is given in fig. 1.
International Journal of Orthopaedics Sciences

Fig 1: Algorithm for the diagnosis of etiology of hyponatremia

| Etiology                  | Cummins K et al. 2014 (n=33 with EPFF) | Henrikus et al. 2016 (n=319, joint replacement) | Our study (n=35, major lower limb fractures) |
|---------------------------|--------------------------------------|-------------------------------------------------|---------------------------------------------|
| Multi factorial           | 72.7%                                | 32.28% (n=103)                                  | 27/35 (77.14%)                             |
| Hypovolemia               | 69.7% (n=23)                         | 6.1% (n=2)                                      | 45.71% (n=16)                              |
| Thiazide diuretics        | 75.8% (n=25)                         | 6.1% (n=2)                                      | 25.71% (n=9)                               |
| CKD/AKI                   | 3.0% (n=1)                           | 3.0% (n=1)                                      | 8.57% (n=3)                                |
| Hypervolemia              |                                      |                                                 | CCF 2                                       |
| Heart failure             | 6.1% (n=2)                           |                                                 | CLD 1                                       |
| Fluid overload            | 3.0% (n=1)                           |                                                 | 8.57% (n=3)                                |
| Drugs                     |                                      |                                                 |                                             |
| Amitryptaline             | 3.0% (n=1)                           | Overall                                          | Overall                                      |
| Sertraline                | 3.0% (n=1)                           | 5.64% (n=18)                                    | 8.57% (n=3)                                |
| Mirtazapine               | 15.2% (n=5)                          |                                                 |                                             |
| Hypotonic fluids          |                                      | 7.83% (n=25)                                    | 2.85% (n=1)                                |
| Undermined                |                                      | 14.10% (n=45)                                   |                                             |

CCF – congestive cardiac failure CLD – Chronic lung disease EPFF – Elderly patients with fragility fractures.

The causes of orthopaedic hyponatremia in the post-operative period include hypovolemia resulting from blood loss after surgery, inadequate fluid replacement, use of diuretics. Surgical process itself (Post-operative pain, nausea, release of cytokines) produces non-osmotic stimulus for AVP release resulting in SIADH. Hypotonic fluid administration, acute kidney injury, medications (thiazide diuretics, SSRIS) and comorbidities (risk factors) can all cause hyponatremia in the post-operative state.

Most common cause of hyponatremia is hypovolemia (hypovolemic hyponatremia) as reported in the recent literature. Cumming K et al. reported hypovolemia as a cause of hyponatremia in 69% of patients and Henrikus et al reported in 33% of the patients in the post-operative period. In our study consistent with literature we found hypovolemia as a causative factor for hyponatremia in 45.71% (n=16). The second common cause is euvolemic hyponatremia (SIADH) as shown in table No.4. Hypervolemia is least common cause and is due to CCF in 2 patients and AKI in 8.57% (n=3) patients.

Table 4: Etiology of hyponatremia

K+ level

| Hypovolemia            | Euvolemia                  | Hypervolemia              |
|------------------------|----------------------------|---------------------------|
| Hypovolemic hyponatremia| SIADH –                    | CCF                       |
|                        | Hypothyroidism-TSH         | CRF/NS                    |
|                        | Cortisol deficiency – morning cortisol | Chronic liver disease |
|                        | Thiazide diuretics        | Fluid overload            |
| Decreased              |                            |                           |
| Vomiting               |                            |                           |
| Diarrhea               |                            |                           |
| Diuretic therapy       |                            |                           |
| Paralytic ileus        |                            |                           |
| Increased              |                            |                           |
| CRF/AKI                | Adrenal insufficiency (AM cortisol) |                           |
| Mineralocorticoid deficiency |                      |                           |

NS – Nephrotic syndrome, CRF – chronic renal failure, AKI – Acute kidney injury.
The diagnosis of etiology of hyponatremia is challenging because multiple mechanisms of hyponatremia may be occurring simultaneously in the post-operative state. ECF volume assessment is very important in the diagnosis of cause of hyponatremia and treatment of hyponatremia. The treatment of hypovolemia and euvolemia (SIADH) are very different. Hypovolemia requires rehydration with sodium containing fluids like 0.9% normal saline, whereas euvolemia requires fluid restriction. Hypervolemia is treated with diuretics. Multiple causes may be present in the same patient and may cause hyponatremia simultaneously.

Avoiding hypotonic and sodium poor solutions (Ringer lactate, 5% dextrose) in the post-operative period can prevent hyponatremia. Similarly avoid unnecessary use of medications associated with hyponatremia during peri-operative period. Once hyponatremia develops, assess the mechanism causing hyponatremia. If the patient is hypovolemic (dehydration), resuscitate with 0.9% normal saline infusion. If the patient is euvolemic with SIADH, fluid restriction is necessary.

Understanding the etiology (mechanism) of hyponatremia in orthopaedic surgical patients and optimal use of (quantity and type of fluids) of intravenous fluids in the perioperative period avoids serious and potentially life threatening complications and improves clinical outcomes.

References
1. Hennrikus E, Ou G, Kinney B, Lehman E, Grunfeld R, Wieler J et al. Prevalence, Timing, Causes, and outcomes of hyponatremia in hospitalized orthopaedic surgery patients. The Journal of Bone and Joint Surgery (American). 2015; 97:1824-1832.
2. Chung H, Kluge R, Schrier RW, Anderson RJ. Post-operative hyponatremia: A prospective study. Arch inter Med. 1986; 146:333-6.
3. Wald R, Jaber BL, Price LL, Upadhyay A, Madias N. Impact of Hospital associated hyponatremia on selected outcomes. Arch inter Med. 2010; 170:294-302
4. Waikar SS, Mount DB, Curhan GC. Mortality after hospitalization with mild, moderate and severe hyponatremia. Am J Med. 2009; 122(9):857-865.
5. Freda BJ, Davidson MB, Hall PM. Evaluation of hyponatremia: A little physiology goes a long way. Cleveland clinic journal of medicine. 2004; 71(8):639-650.
6. Milionis HT, Liamis GL, Elisaf MS. The hyponatremic patient: a systematic approach to laboratory diagnosis. CMAJ. 2002; 166(8):1056-1061.
7. Assadi F. Hyponatremia: a problem solving approach to clinical cases. J Nephrol. 2012; 25(04):473-480.
8. Chung HM, Kluge R, Schrier RW, Anderson RJ. Clinical assessment of extracellular fluid volume in hyponatremia. American journal of medicine. 1987; 83:905-908.
9. Robertson GL. Antidiuretic hormone. Normal and disordered function. Endocrinol Metab Clin North Am. 2001; 30(3):671-94
10. Caramel C, Molina M, Tejedor A. Regulation of post-operative water excretion: a study on mechanisms. J Am Soc Nephrol. 2002; 13:654A.
11. Philbin DM, Emerson CW, Coggins CH, Moss JM, Slater E, Schneider RC. Renin catecholamine and vasopressin response to stress of anesthesia and surgery?. Anesthesiology. 1979; 51(3):S122.
12. Shapiro DS, Sonnenblick M, Galpherin I, Melkonyan L, Munter G. Severe hyponatremia in elderly hospitalized patients; prevalence, etiology and outcome. Inter Med J. 2010; 40(8):574-580.
13. Cumming K, Hoyle GE, Hutchison JD, Soiza RL. Prevalence, incidence and etiology of hyponatremia in elderly patients with fragility fractures. PLOS one. 2014; 9(2):e 88272.
14. Anderson RJ, Chung HM, Rudijer K, Schrier RW. A prospective analysis of its epidemiology and the pathogenetic role of vasopressin. Ann intern Med. 1985; 102:164-8.
15. Ellison DH Berl T. The syndrome of inappropriate antidiuresis. N Engl J Med 2007; 356(20):2064-2072.
16. Elisaf MS, Milionis HJ, Siamopoulos KC. Electrolyte abnormalities in elderly patients admitted to a general medical ward. Geriatr Nephrol Urol. 1991; 7:73-9.
17. Decaux G, Schiesser M, Coffernils M, prosperf F, Namiias B, Brimouilles et al. Uric acid anion gap and urea concentration in the diagnostic approach to hyponatremia. Clin Nephrol. 1994; 42(2):102-8.