Oliguria, Volume Overload, Na\textsuperscript{+} Balance, and Diuretics

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Disorders of body fluids and electrolytes are among the most common problems that are encountered in the critical care setting. This article outlines the pathophysiology and treatment approach to fluid overload and dysnatremias that frequently accompany the fluid overloaded state.

Water and fluid homeostasis

Because body water is the primary determinant of the osmolality of the extracellular fluid (ECF), disorders of body water homeostasis can be divided into hypo- and hyperosmolar disorders, depending on whether there is an excess or deficiency of body water relative to body solute. Depending on sex, age, and body fat, water constitutes 55\% to 65\% of body weight and is distributed between the intracellular fluid and the ECF in a 2:1 ratio. Of the ECF, three fourths is interstitial and one fourth is intravascular (circulating blood volume) [1]. Because biologic membranes are freely permeable to water, osmotic pressure is kept equal between all compartments. Water metabolism represents a balance between the intake and excretion of water. Thirst that is stimulated by intravascular hypovolemia and hyperosmolarity is our primary defense against severe reduction of total body water.

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0749-0704/05 see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.ccc.2005.01.009
Circulating blood volume is regulated by a feedback system through volume sensors that are located in the carotid sinus, the atria, and the afferent arteriole of the kidney. The end result of any change in circulating blood volume is a change in sodium excretion by the kidneys that is brought about by activation of the sympathetic nervous system, the renin-angiotensin-aldosterone axis, and release/suppression of natriuretic peptides. The intravascular volume stimuli also affect the release of arginine vasopressin (AVP) which is the prime determinant of free water excretion by the kidneys. Clinical fluid overload thus results from an overcompensatory increase in sodium and water retention due to disease states by the above mechanisms. The consequent disruption of the Starling forces that regulate fluid transfer between the intravascular and interstitial compartments results in fluid efflux that causes edema, ascites, pleural effusions, and so forth (ie, "third spacing"). This, in turn, may result in a relative decrease in intravascular circulating blood volume and lead to insufficient perfusion and organ dysfunction.

Assessment of volume overload in the ICU

Volume overload is a common occurrence in the critically ill and is manifested by physical findings, such as edema, anasarca, pleural effusions, and ascites. Usually, the clinical dilemma is deciding if these patients have an underlying increase in effective circulating blood volume that would prompt specific fluid removal therapies. Traditional indicators of hydration status and tissue perfusion, such as systemic blood pressure, heart rate, body weight, jugular-venous pulsation (JVP), and peripheral edema, can provide important clues about which appropriate interventions can be made. In the ICU, however, some of these indicators are less useful for a variety of reasons.

The JVP is not an accurate surrogate for right ventricular filling pressures in the presence of positive pressure ventilation, especially with positive end-expiratory pressure. Blood pressure and heart rate are affected by numerous physiologic and treatment variables in the ICU and are unreliable measures of volume status. In the ICU, it is common to assume that one can obtain a more accurate assessment of preload by measuring the central venous pressure (CVP) or pulmonary capillary occlusion pressure (PAOP); however, this is only the case when these pressures are low (<10 mm Hg). An increased CVP or PAOP does not ensure adequate filling pressures. Volume variables, such as total end diastolic volume index and intrathoracic blood volume index may be more useful indicators than pressure variables (eg, CVP, PAOP) for assessment of extravascular lung water index in septic patients who have pulmonary edema, but lack widespread clinical availability [2].

Response to a single fluid challenge or multiple fluid challenges may not detect hypovolemia, depending on its degree. The presence of a cardiac index that is greater than 3.0 L/min/m² generally suggests adequate preload but it may not reflect optimal preload. The mixed venous oxygen saturation can serve as a surrogate for cardiac output, but again, does not define optimal filling. In patients who are on mechanical ventilation, the absence of arterial pulse-pressure variation provides a robust indicator of fluid loading. Pulse pressure variation was shown to be a better predictor of fluid responsiveness in patients who underwent coronary artery bypass graft in a small study [3]. In other cases, echocardiography may provide the only reliable evidence of fluid optimization and may alter therapy further, even in the presence of a pulmonary artery catheter [4].

Additional information may be obtained by chest radiography, which may reveal an enlarged heart, pulmonary interstitial edema (Kerley B lines), or pulmonary vascular engorgement. An additional piece of data from a chest radiograph, the vascular pedicle width (VPW)—the mediastinal silhouette of the great vessels—can aid in the assessment of patients' intravascular volume status. The objective measurement of the VPW, obtained from upright or supine chest radiographs, can increase the accuracy of the clinical and radiographic assessment of intravascular volume status by 15% to 30%; this value may be even higher when VPW is used serially within the same patient. Regardless of the presence or absence of pulmonary edema, the best VPW cutoff for differentiating a high versus normal to low intravascular volume status is 70 mm. Patients who

**Box 1. Pathogenesis of hyper- and hypo-osmolar states**

**Hyperosmolar disorders**

**Water depletion**

**Hypotonic fluid loss**

- Diabetes insipidus (central and nephrogenic)
- Renal loss (osmotic diuresis, diuretic therapy, postobstructive diuresis)
- Nonrenal loss (gastrointestinal, cutaneous, pulmonary, peritoneal dialysis)

**Solute excess**

- Excess sodium administration
- Hyperalimentation

**Hypo-osmolar disorders**

- Excess water intake
- Solute depletion

- Renal solute loss (diuretic therapy, hyperglycemia, mannitol, salt wasting nephropathy, mineralocorticoid deficiency)
- Nonrenal solute loss (gastrointestinal, cutaneous, blood loss)

**Solute dilution**

- Increase proximal nephron reabsorption (cirrhosis, congestive heart failure, nephritic syndrome, hypothyroidism)
- Impaired distal nephron dilution (syndrome of inappropriate anti-diuretic hormone, glucocorticoid deficiency)
Hyponatremia can be classified into three types according to effective plasma osmolality: hyper-osmolar, normo-osmolar, and hypo-osmolar. In the critical care setting, hypo-osmolar hyponatremia accounts for most of the water and solute imbalance (see Box 1).

**Hypo-osmolar hyponatremia**

The most important mechanism in the pathogenesis of hypo-osmolar hyponatremia is retention of water; this usually reflects the presence of conditions that impair renal excretion of water. In a minority of cases, it is caused by excessive water intake, with a normal or nearly normal excretory capacity [8].

Conditions of impaired renal excretion of water, with the exception of renal failure, are characterized by high plasma concentrations of AVP, despite the presence of hypotonicity [15]. The two most common causes of hyponatremia are effective circulating volume depletion and the syndrome of inappropriate antidiuretic hormone (SIADH) secretion. Although patients who have heart failure or cirrhosis have increased plasma volume, the pressure that is sensed at the carotid sinus baroreceptors is reduced as a result of the decrease in cardiac output (in heart failure) or peripheral vasodilatation (in cirrhosis). The AVP levels vary with the severity of the underlying disease. Conversely, hyponatremia in the nephrotic syndrome is more likely to be due to the renal disease, than to the underfilling that is induced by hypoalbuminemia.

SIADH causes hyponatremia by excessive and inappropriate retention of water. An increase in vascular volume that is caused by retention of water stimulates the kidney to excrete salt and water to restore blood volume to normal levels. Although salt is excreted, water is retained by AVP, and thus, leads to hyponatremia. SIADH can be caused by tumors, intrathoracic causes, central nervous system abnormalities, or multiple drugs.

Finally, hyponatremia can occur in patients who have hypothyroidism or adrenal insufficiency; the lack of cortisol is responsible for the hyponatremia. Finally, advanced renal failure and primary polydipsia can cause hyponatremia, despite suppression of AVP release [16,17].

Water restriction to less than that of water output is the primary therapy for hyponatremia in edematous states (eg, heart failure, cirrhosis), SIADH, primary polydipsia, and advanced renal failure. Isotonic saline should be given to patients who have true volume depletion or adrenal insufficiency, whereas hypertonic saline should be administered only in cases of symptomatic hyponatremia. In hypovolemic patients, isotonic saline corrects the hyponatremia by increasing the plasma sodium by 1 mEq/L to 2 mEq/L for every liter of fluid infused. As volume repletion removes the stimulus to AVP, release excess water is excreted.

Rapid correction of sodium in patients who have hyponatremia may result in cerebral demyelination, and therefore, is contraindicated. The risk increases with the chronicity of the condition; patients who have chronic asymptomatic hyponatremia should be corrected slowly. Although the optimal rate of correction has not been defined clearly, the recommendation in asymptomatic patients is that

Hyponatremia

Sodium is the most predominant plasma cation; under normal conditions, it is regulated in the narrow range of 135 mmol/L to 145 mmol/L. Along with chloride, urea, and glucose, it accounts for 86% of the ECF osmolality.

Hyponatremia is a common disorder; it occurs in up to 3% to 6% of hospitalized patients and it is especially prevalent among critically ill patients [6-8]. It represents an excess of body water relative to body sodium and can be a clinical complication of a wide variety of diseases, surgical procedures and medications; thus, a systemic approach to the diagnosis is essential.

Usually, patients whose serum sodium levels are greater than 120 mmol/L to 125 mmol/L are asymptomatic; however, those who develop hyponatremia rapidly or have even lower levels can develop a variety of symptoms, such as headache, nausea, vomiting, cognitive impairment, lethargy, restlessness, and confusion [9]. In addition, muscle cramps and noncardiogenic pulmonary edema can occur [10]. Severe complications include seizures, coma, permanent brain damage, respiratory arrest, brainstem herniation, and death [11,12].

The neurologic symptoms are caused by changes in brain cell volume that are driven by high intracellular osmolality relative to ECF. The relative increase in intracellular osmoles causes hypertonic ECFs to shift intracellularly, and thus, cause cellular swelling and increased brain volume [13]. In the presence of hyponatremia, there is a gradual decrease in intracellular osmolality so that if the decrease in ECF osmolality is slow, cell size is affected less severely. In these patients, the main risk of complications occurs during the correction phase.

Approximately 70% of cases of hyponatremia are hospital-acquired, thus one must be aware of potential risk factors. Impaired age, impaired renal function, circulating volume depletion, congestive heart failure, cirrhosis, intravascular fluids, and medications, especially diuretics, frequently are associated with the development of hyponatremia. The elderly population is particularly susceptible to hyponatremia. This is multi-factorial as a result of the decrease in renal function, decline in glomerular filtration rates, limitation of sodium conservation, and exposure to multiple medications with the decreased ability to withstand disease-related and iatrogenic insults [14].
the plasma sodium concentration be increased at a maximum rate of 10 mEq/L/d to 12 mEq/L/d (~0.5 mEq/L/h) [18–20]; however, even at this rate, some patients may develop neurologic symptoms.

More aggressive initial correction, at a rate of 1.5 mEq/L/h to 2 mEq/L/h, is indicated for the first 3 to 4 hours or until the symptoms resolve in patients who present with seizures or other severe neurologic abnormalities [19–21]. Even in such a scenario, the plasma sodium concentration probably should not be increased by more than 12 mEq/L in the first 24 hours, because partial cerebral adaptation likely has occurred [22].

Hyperosmolar hyponatremia

Hyperosmolar hyponatremia can be caused by an increase in osmotically active solutes like glucose, mannitol, or sorbitol. A change of each 100 mg in glucose decreases sodium by 1.5 mEq/L; however, patients in critical care units frequently have significant alterations in body water (ascites, edema) that may result in an inaccurate prediction of changes in serum sodium. Hyponatremia that is caused by mannitol or sorbitol essentially is limited to irrigating fluids that are used during transurethral resection of the prostate (TURP) or a bladder tumor, and endoscopic hysteroscopy, where nonconductive flushing solutions contain glycine, sorbitol, or mannitol [23,24]. The incidence of hyponatremia following TURP is approximately 7% [25]. Risk factors for severe hyponatremia are prolonged surgery, large tissue resection, and excess height of the irrigant solution reservoir, which introduces the fluid under high pressure [23]. The use of glycine irrigant solutions during hysteroscopy in women can produce similar complications [26].

No specific therapy is necessary in the absence of symptoms. Hypertonic saline can be given if the plasma osmolality is reduced, but is not likely to be effective when the plasma osmolality is in the normal range [27]. Hemodialysis, which corrects the hyponatremia and removes glycine and its toxic metabolites, has been used in two settings: in patients who have end-stage renal disease who have no other means to excrete the excess solute and water, and in patients who have severe, persistent symptoms, marked hyponatremia, and a normal plasma osmolality [24,28].

Normo-osmolar hyponatremia

Normo-osmolar hyponatremia is caused by accumulation of cations in the ECF or by pseudohyponatremia [29]. Pseudohyponatremia that is due to in vitro hemolysis is more common. The Na⁺ concentration is lower in the red blood cells, and hence, when cells lyse pseudohyponatremia develops. The release of hemoglobin during hemolysis further decreases Na⁺ concentration. Hypertiglidemia and hyperproteinemia are rare causes of hyponatremia [29].

Hypernatremia

Although an excess of body sodium can cause hypernatremia, most cases are due to losses of body water in excess of body solutes. This is the result of insufficient water intake or excessive water excretion. Hypernatremia is synonymous with hyperosmolality. The pathogenesis of hypernatremia, besides insufficient water intake, includes hypotonic fluid loss to renal, gastrointestinal, cutaneous, or pulmonary causes. Causes of renal losses are listed in Box 1. The primary goal of therapy is to replenish intravascular volume adequately.

Oliguria

Several definitions for oliguria can be found in the literature, which generally range from a urine output of less than 200 mL to 500 mL in 24 hours. To standardize the use of the term across different studies and populations, the Acute Dialysis Quality Initiative recently adopted a definition of oliguria as urine output of less than 0.3 mL/kg/h for at least 24 hrs (www.ADQI.net).

Given the lack of consensus over definitions until now, it is difficult to determine the incidence of oliguria. Some studies estimated that up to 18% of patients in the medical-surgical ICU who have intact renal function exhibit episodes of oliguria [30]. Further, 69% of patients in the ICU who develop acute renal failure (ARF) are oliguric [31]. Overall, ARF in the ICU has a poor prognosis (mortality rates range from 30%-70%) and oliguric ARF is associated with a worse outcome than nonoliguric ARF. Thus, it is essential to understand the physiologic derangements that lead to this exceedingly common problem.

Pathophysiology

Urinary output is a function of glomerular filtration, tubular secretion, and reabsorption. Glomerular filtration is directly dependent on renal perfusion. This, in turn, is a function of arterial pressure and renal vascular resistance. The intrarenal vasculature is capable of preserving the glomerular filtration rate (GFR) in the case of varying systemic pressure through important neurohormonal auto-regulating mechanisms that affect the afferent and efferent arterioles; the renin-angiotensin-aldosterone system may be the most significant (Fig. 1). Oliguria indicates a dramatic reduction in GFR or a mechanical obstruction to urine flow.

Reduction in glomerular filtration rate

Oliguria that is secondary to a decrease in GFR usually is related to one of the following four conditions: (1) an absolute decrease in intravascular volume that is due to trauma, hemorrhage, burns, or diarrhea or sequestration of fluid
Mechanical obstruction

Oliguria that is secondary to mechanical obstruction can be subclassified according to the anatomic site of the obstruction. Tubular-ureteral obstruction may be caused by stones, papillary sloughing crystals, or pigment. Urachal or bladder neck obstruction, is usually more common and typically is due to prostatic hypertrophy or malignancy. Finally, a malpositioned or obstructed urinary catheter also can result in mechanical obstruction.

Diagnostic approach to oliguria

Oliguria is associated with considerable morbidity and mortality; however, merely reversing oliguria, particularly by the use of diuretic agents, does not improve outcome. Thus, rapidly determining the cause of oliguria is essential.

Rule out urinary obstruction

The initial step in diagnosis is to rule out urinary obstruction before embarking on a lengthy work-up for prerenal versus intrarenal causes of renal insufficiency. A history of prostatic hypertrophy may provide some clues to the presence of distal obstruction. In the ICU setting, however, distal obstruction that presents as oliguria is common as a result of obstruction of the urinary catheter (especially in male patients). Hence, in patients who have new-onset oliguria, the urinary catheter must be flushed or changed to rule out obstruction. Although uncommon in the acute setting, complete or severe partial bilateral ureteral obstruction also may lead to acute, "acute on chronic," or chronic renal failure. Early diagnosis of urinary tract obstruction is important, because many cases can be corrected; a delay in therapy can lead to irreversible renal injury. Renal ultrasonography usually is the test of choice to exclude obstruction [33]. It is noninvasive, can be performed at the bedside, and has the advantage of avoiding the potential allergic and toxic complications of radiopaque contrast media. In most affected patients, it can diagnose hydronephrosis and establish its cause; it also can detect other causes of renal disease, such as polycystic kidney disease. Under some circumstances, however, renal ultrasonography may not yield good results. For example, in early obstruction or obstruction that is associated with severe dehydration, hydronephrosis may not be seen on initial ultrasound, but may appear on an ultrasound that is done later in the course of the disease. CT scanning should be performed if the ultrasound results are equivocal, if the kidneys cannot be well-visualized, or if the cause of the obstruction cannot be identified.

Laboratory indices

Some authorities advocate examining the urine sediment, whereas others do not. Although hyaline and fine granular casts are common in prerenal disease, acute tubular necrosis usually is associated with coarse granular casts and tubular...
Table 1: Biochemical indices useful to distinguish prerenal from intrarenal acute renal failure

<table>
<thead>
<tr>
<th></th>
<th>Prerenal</th>
<th>Renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osm U (mOsm/kg)</td>
<td>&gt; 500</td>
<td>&lt; 400</td>
</tr>
<tr>
<td>Na U (mmol/L or mEq/L)</td>
<td>&lt; 20</td>
<td>&gt; 40</td>
</tr>
<tr>
<td>Scr/creatinine</td>
<td>&gt; 0.1</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>U/S creatinine</td>
<td>&gt; 40</td>
<td>&lt; 20</td>
</tr>
<tr>
<td>U/S osmolality</td>
<td>&gt; 1.5</td>
<td>&gt; 1</td>
</tr>
<tr>
<td>FeNa (%)</td>
<td>&gt; 2</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Fe urea (%)</td>
<td>&lt; 25</td>
<td>&gt; 25</td>
</tr>
</tbody>
</table>

Abbreviations: Osm, osmolality; S, serum; U, urine.

*([U Na / S Na] / [U creatinine / S creatinine]) × 100.

epithelial casts; however, the discriminating ability of these findings is of limited practical value. The main reason for examining the urine sediment is the detection of red cell casts which indicate glomerular disease. The urine sediment in post-renal failure often is bland; generally, no casts or sediments are seen. Occasionally, a few red cells and white cells (eg, renal calculi or infection) may be seen. Eosinophilia or eosinophiluria may be seen with interstitial nephritis or atheroembolic disease; the latter also may exhibit hypocomplementemnia [34].

Table 1 lists the laboratory values that are of use in distinguishing prerenal causes of ARF from intrarenal causes of ARF. A fractional excretion of sodium of less than 1 traditionally has been used as a marker for a prerenal cause of oliguria. These indices are unreliable after the patient has received diuretic or natriuretic agents (including dopamine and mannitol) and also may be confounded by endogenous osmolar substances, such as glucose or urea.

Treatment of oliguria and fluid overload

The mainstay of treatment of oliguria is the identification and correction of the precipitating factors; supportive measures, such as avoidance of nephrotoxic agents and dose adjustment of renally-excreted drugs; and ensuring adequate renal perfusion. The last involves correction of hypotension and appropriate intravascular volume expansion. Correction of hypotension is especially crucial because in sepsis and ischemic renal failure, some of the important autoregulating mechanisms that help to preserve GFR in the case of fluctuating blood pressures are disrupted. In these patients, renal blood flow is related directly to systemic arterial pressure; vasoactive drugs may be necessary in the ICU setting to increase the mean arterial pressures to more than usual values to maintain adequate renal perfusion pressures and adequate urine output [35]. In patients who have chronic hypertension and renal vascular disease, the auto-regulation curves are shifted to the right, and therefore, a greater arterial pressure may be required to ensure adequate renal perfusion. One must ensure that the patient is volume resuscitated adequately before initiation of these vasoactive drugs; in many instances, initial treatment consists of fluid challenges in the hope of correcting unrecognized volume depletion. The ideal blood pressure to aim for must be individualized based on factors, such as the patient’s premorbid blood pressure and the presence of vascular disease. Hemodynamic monitoring devices may provide important clues about the intravascular volume status that may enable a more streamlined, “goal-directed” approach to therapy.

Diuretics are used commonly in the ICU setting to treat fluid excess and for maintaining urine flow in the setting of oliguria. From a physiologic standpoint, treating ECF excess in the absence of intravascular hypervolemia is not justifiable. The third spacing of fluids is mostly a cosmetic issue, except for instances like the abdominal compartment syndrome where acute tense ascites may impact venous return, diminish renal perfusion, and impair lung compliance.

Traditionally, diuretics have been used in the early phases of oliguria to “jump start” the kidney and to establish urine flow. Presumably, the absence of oliguria makes it easier to regulate volume status. Because nonoliguric renal failure generally has a better prognosis, clinicians frequently use diuretics in this setting. A study by Anderson et al [36] in 1977 claimed a reduction in mortality from 50% to 26% by using high-dose loop diuretics to convert oliguric renal failure to nonoliguric renal failure. This study excluded patients who had shock and perioperative renal failure. These results have not been reproduced in more recent trials. A study in 1997 by Shilliday et al [37] examined the effect of loop diuretics, in patients who had ARF, on the incidence of renal recovery, dialysis, and death. Although loop diuretics did result in diuresis, there was no difference in the above outcomes when compared with placebo. Two other randomized controlled trials did not show any benefit on survival with the use of loop diuretics in oliguric renal failure [38,39]. The Project to Improve Care on Acute Renal Disease (PICARD) Study Group reported the results of a large cohort study of critically ill patients who had ARF from 1989 to 1995. Diuretic use was associated with a significant increase in the risk of death or nonrecovery of renal function. Although this may or may not be causal, it is unlikely that the use of diuretics in the setting of oliguria affords any benefit [40]. A more recent collaborative, multi-national epidemiologic study did not find an increase in mortality with diuretics, although it failed to show any benefit [41]. Thus, in the absence of a proven benefit and the suggestion of harm, aggressive diuretic therapy is best avoided in the critically ill patient unless it is indicated for the treatment of clinically significant pulmonary edema. There also is no documented benefit of coadministration of albumin with loop diuretics in ECF overloaded patients who are hypalbuminemic.

Renal replacement therapy has been the focus of a large amount of research in recent years as a means to alleviate volume overload in disease states (eg, heart failure, sepsis). In addition, there are data to suggest that large volume hemofiltration (ultrafiltration >2 L/h) may result in improved clearance of cytokines in septic patients [42]. Although this approach to blood purification in sepsis seems logical, promising, and opens new perspectives, many questions remain unanswered, including the timing, duration, and frequency of these therapies in the clinical setting.
Summary

The presence of oliguria should alert the clinician to undertake a diligent search for any correctable underlying causes. The mainstay of treatment is to ensure adequate renal perfusion through optimization of cardiac output and volume status. The use of diuretics and vasoactive agents, although common, is not supported by the evidence; emerging data suggest that they may cause harm.

References