

Don't just do something, stand there!

Ralph Kettritz and Friedrich C. Luft

Department of Nephrology and Critical Care Medicine, Charité Medical Faculty, Virchow Klinikum Campus, and Experimental and Clinical Research Center, Berlin, Germany

Correspondence and offprint requests to: Friedrich C. Luft; E-mail: luft@charite.de

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Hyponatraemia must be assessed in a predictive fashion. Will my patient get worse? Or will my patient recover simply by observation? The effective water clearance (EWC) is the key. Its estimation requires only determining the urine sodium and potassium levels.

Case

Physicians are under tremendous pressure to act, especially in emergencies. 'Don't just stand there, do something! After all, you're a doctor!', is a common admonition. Nevertheless, oftentimes the best action is inaction. 'Watchful waiting' is the term used for this strategy. Physicians should be familiar with clinical tools to decide which of both strategies is appropriate in a given situation. A 68-year-old disoriented woman was admitted to our emergency room at 18:00 in the evening. She was awake, but hardly aware and could not follow simple commands. There were no localizing neurological findings. She had undergone a complex tooth extraction that morning. She had a known platelet disorder and had been prepared with 4 µg/kg desmopressin infusion at the recommendation of a haematologist. Her blood pressure was normal. Her only medication was trimipramine, which she took since the death of her dachshund 1 month earlier. The serum sodium concentration was 118 mmol/L, potassium 3.6 mmol/L, glucose 8 mmol/L, urea nitrogen 4 mmol/L and serum creatinine 45 µmol/L. We concluded that her disordered mental status was related to acute hyponatraemia.

Question

What further diagnostic tests would you order; what treatment would you initiate; what is the differential diagnosis of her peripheral smear? (Table 1).

Answer

Trimipramine can cause hyponatraemia; however, our suspicion in this acute case was desmopressin. We

measured sodium and potassium levels in urine. Since the sum of these two effective osmoles was less than her serum sodium concentration, her effective free water clearance had to be positive and her serum sodium would increase without treatment. The house staff had not measured urine osmolality in the emergency department (they should have), but we reasoned that with such a low concentration of electrolytes in her urine, the urine had to be dilute, indicating that the desmopressin effect was wearing off.

The rate at which plasma is cleared of solute is the osmolar clearance (Cl); and the rate at which plasma is cleared of solute-free water is the free water clearance. Since urine flow is determined by the rate at which plasma is cleared of solutes and water, urine flow (V) is given as the sum of osmolar (C_{osm}) and free water clearance (Cl_{H₂O}):

$$UV = C_{\text{osm}} + Cl_{\text{H}_2\text{O}} \quad (1)$$

Rearranging this equation yields Cl_{H₂O}

$$Cl_{\text{H}_2\text{O}} = UV - C_{\text{osm}} \quad (2)$$

Since osmolar clearance is given as the product of urine flow rate and the ratio of urine-to-plasma osmolality, this is commonly represented as

$$Cl_{\text{H}_2\text{O}} = V - (U_{\text{osm}} \times UV) \quad (3)$$

Knowing Cl_{H₂O} is good, but we are concerned about the serum sodium concentration. Since some osmolytes (urea for example) can diffuse across cell membranes given sufficient time, they are not 'effective' in the sense that they contribute to tonicity and thereby influence the sodium concentration. The effective cations are sodium (extracellular) and potassium (intracellular). We can more practicably calculate the EWC [1]. We know from the Edelman equation [2] that sodium, potassium and total body water (TBW) determine the serum (S) sodium concentration: $S_{\text{Na}^+} \approx (\text{Na}^+ + \text{K}^+)/\text{TBW}$. Thus, only sodium and potassium levels play a role in our considerations. Admittedly, life is not quite that simple, and the interested reader can pursue the subject further [3]. However, for

Table 1. Serum and urine values (mmol/L) over a timeframe of 38 h

Time	18:00	06:00	21:00	08:00
	Glucose 5% infusion			
Serum				
Sodium	118	125	138	138
Potassium	3.6	3.0	5.4	4.4
Urine				
Sodium	16	–	24	43
Potassium	7	–	9	16

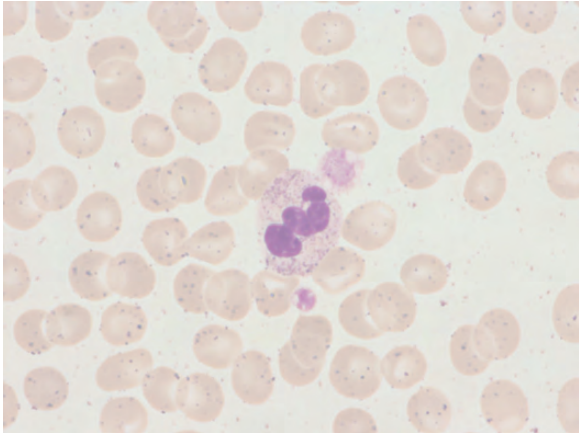


Fig. 1. An oil-immersion field showing a normal neutrophil flanked by two giant platelets. Ignore the grunge; it is an artefact and she did not have basophilic stippling!

clinical purposes we can calculate EWC as follows:

$$\text{EWC} = ([\text{UNa}^+ + \text{UK}^+] \times \text{UV}) / \text{SNa}^+ \quad (4)$$

This relationship provides us with a very powerful tool. We see from the relationship that if $\text{UNa}^+ + \text{UK}^+ < \text{SNa}^+$, then SNa^+ must increase. Similarly, if $\text{UNa}^+ + \text{UK}^+ > \text{SNa}^+$, then SNa^+ must decrease. Hence, with any spot urine specimen we can easily determine what happens next. Clinicians commonly only measure the urine sodium and not both urine sodium and urine potassium. This practice is an error!

Most hyponatraemias are drug (physician) induced, as was the case here [4]. Acute hyponatraemia should be corrected rapidly, because acute hyponatraemia can cause neurological complications [5]. The appropriate treatment is withdrawing the offending agent. Estimating the EWC and the ratio between $\text{SNa}^+ / [\text{UNa}^+ + \text{UK}^+]$ allows predicting the spontaneous SNa^+ course. Using this tool, we knew that our patient would get better without further measures. Had 3% saline solution been infused, as advocated for acute symptomatic hyponatraemia, the rate of increase in the serum sodium would have been even faster. Instead, glucose 5% was infused to delay the rate of increase. As a matter of fact, desmopressin has been used therapeutically for the same purpose, even in

a patient with desmopressin-induced hyponatraemia [6, 7]. Conceivably, central pontine myelinolysis might have ensued with 3% saline and more rapid correction. However, myelinolysis is actually more associated with correction of chronic, rather than acute, hyponatraemia—probably because the pathophysiology of chronic hyponatraemia is different from that of acute hyponatraemia. Central pontine myelinolysis has not been reported after correction of acute hyponatraemia to our knowledge.

Our patient had the Bernard–Soulier syndrome (BSS), also called haemorrhagiparous thrombocytic dystrophy. BSS is a rare autosomal recessive coagulopathy that causes a deficiency of glycoprotein Ib, the receptor for von Willebrand factor, which is important in clot formation. BSS is a giant platelet syndrome and is characterized by abnormally large platelets. For patients affected by severe inherited platelet dysfunctions including BSS, platelet transfusion is frequently needed for controlling spontaneous bleeding, and is always needed when trauma occurs or surgery is performed [8]. Desmopressin, increases plasma levels of von Willebrand factor and factor VIII giving rise to increased platelet adhesiveness and aggregation associated with shortened bleeding time, has also been employed. However, patients must be counselled and monitored until the pharmacological effects on urine concentration have subsided (Figure 1).

Conflict of interest statement. None declared.

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