Assessing the degree of extracellular fluid volume contraction in a patient with a severe degree of hyperglycaemia

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Case

A 7-year-old, 20 kg female had a 2 week history of polydipsia, polyuria and a weight loss of ~2.5 kg. She was drowsy, but easily roused and answered questions appropriately. Blood pressure was 100/60 mmHg, heart rate 148/min, respiratory rate 12/min, capillary refill >3 s and tissue turgor was poor. There was no urine output in the first 2 h (a Foley catheter was inserted). Laboratory data are summarized in Table 1. Based on this information, 98 adult and paediatric medical specialists were asked to assess her degree of extracellular fluid (ECF) volume contraction (Table 2).

Assessing the ECF volume

It is difficult to quantitate the degree of ECF volume contraction on clinical grounds [1–3]. Therefore, laboratory data were examined to help in this regard (Table 1).

Haematocrit

When normal, her blood volume would be ~1.5 l (75 ml/kg). With a haematocrit of 40%, her red blood cell (RBC) volume would be 0.61 l and plasma volume 0.91 l (Equation 1). In contrast, with a haematocrit of 61% and the same RBC volume, her blood volume would be ~1 l. Thus, with the same 0.61 l RBC volume, her plasma volume would be 0.41 l, reduced by >50%. Only 16/98 respondents to our survey used the haematocrit to assess the degree of ECF volume contraction (Table 2).

\[
\text{Haematocrit} = \frac{\text{RBC volume}}{\text{total blood volume}} \quad (1)
\]

Venous PCO₂

Normally, the venous PCO₂ is ~6 mmHg greater than the arterial PCO₂. With a low cardiac output, there is a disproportionate rise in venous PCO₂ [5]. On admission, her venous PCO₂ was 69 mmHg (arterial PCO₂: 43 mmHg), implying a very low blood flow rate. No respondent used the venous PCO₂ to help assess the circulating volume and its response to therapy.

Oliguria

The extreme degree of hyperglycaemia (P_Glu) and oliguria together with the modest elevation in plasma creatinine concentration (Table 1) suggested a recent but marked fall in glomerular filtration rate (GFR)—its likely basis was very poor renal perfusion. Perhaps

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The authors wish it to be known that, in their opinion, all of the authors contributed equally to this work.

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her high blood viscosity decreased flow, especially in the smaller arterioles.

**Deficit of Na**

The ECF Na deficit was >50% because of ECF volume contraction (>50%) and the PNa of 129 mM (Table 1). Virtually all respondents thought that the Na deficit must be much smaller because of the absence of hypotension (Table 2).

**Basis for the extreme degree of hyperglycaemia**

Hyperglycaemia is due to either more glucose in the ECF compartment and/or a low ECF volume. Had her GFR been only 20% of normal (0.33 l/h) for the initial 3 h in hospital, she would have excreted almost half of her ECF glucose content [11 × (110 – 10) mM or 100 mmol vs an ECF glucose content of 220 mmol on admission (2 l × 110 mM)]. A 50% decline in ECF volume raised her P_Glu 2-fold. Hence, with the same glucose input from her gastrointestinal tract, the very low ECF volume and GFR could virtually quadruple her P_Glu from 500 (27.5 mM) to 2000 mg/dl (110 mM).

**Hyperglycaemia and the ECF volume**

Hyperglycaemia leads to a higher ECF volume because glucose is an effective osmole for skeletal muscle [6]. Using an imaginary redistribution, her ECF was divided into two iso-osmotic solutions because the glucose-containing one will be excreted rapidly when the GFR rises. For this calculation, we assumed that the glucose solution had a PGlu equal to her effective plasma osmolality (P_osm) – 368 Osm/kg H2O in 0.6 l (220 mmol/368 mmol/l). The other 1.4 l contains all the Na with an identical P_osm [P_Na 184 mM (one-half of 368 mM)]. Hence, this severe degree of hyperglycaemia permitted her to have an ECF volume that was 30% higher than it would have been in the absence of hyperglycaemia [7].

**Normal P_HCO3**

Her low HCO₃⁻ content (25 mM × one-half ECF volume) and increased plasma anion gap suggested that she had ‘occult’ metabolic acidosis. The increase in plasma anion gap was magnified by ECF volume contraction. Because her plasma l-lactate⁻ was 0.9 mM, we suspected that she had diabetic ketoacidosis; unfortunately, her plasma β-HB⁻ concentration was not measured.

**Treatment**

**Therapy for ECF volume contraction**

The patient received a bolus of 160 ml saline over 80 min—her venous PCO₂ fell to 47 mmHg (Figure 1). Unfortunately, the haematocrit was not measured at this time. Because there was no urine output, there was a 2 ml/min net rise in her ECF volume. This infusion should lower the viscosity of arterial blood to a greater extent, because on first pass it has not reached systemic capillaries. Over the next 120 min, 235 ml of isotonic saline was infused and 200 ml of urine was excreted. Hence, her net fluid gain was only 0.3 ml/min and her venous PCO₂ rose to 67 mmHg with no change in arterial PCO₂. Of note, her urine output declined appreciably. This venous PCO₂ change illustrates the initial benefit of re-expanding the arterial plasma volume and its abrogation by a marked decline in the rate of net fluid addition to this compartment.

Two of the important risk factors for cerebral oedema are a rapid rate of infusion of saline and a large fall in the effective P_osm [8–10].

**Rate of infusion of saline.** Because she was awake and responded appropriately to questions, her cerebral

### Table 1. Laboratory data on admission

<table>
<thead>
<tr>
<th>Plasma (venous)</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>2000 mg/dl (110 mM)</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.19</td>
<td></td>
</tr>
<tr>
<td>P_WCO₂</td>
<td>25 mM</td>
<td></td>
</tr>
<tr>
<td>P_CO₂</td>
<td>69 mmHg</td>
<td></td>
</tr>
<tr>
<td>Na</td>
<td>129 mM</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>7.3 mM (haemolysed)</td>
<td></td>
</tr>
<tr>
<td>Cl</td>
<td>80 mM</td>
<td></td>
</tr>
<tr>
<td>White blood cells</td>
<td>10.6 × 10⁹/l</td>
<td></td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>17.8 g/dl</td>
<td></td>
</tr>
<tr>
<td>Haematocrit</td>
<td>61%</td>
<td></td>
</tr>
<tr>
<td>Platelets</td>
<td>154 × 10⁹/l</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.9 mg/dl (82 μM)</td>
<td></td>
</tr>
<tr>
<td>Urea</td>
<td>28 mg/dl (10 mM)</td>
<td></td>
</tr>
<tr>
<td>Plasma (arterial)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P_CO₂</td>
<td>43 mmHg</td>
<td></td>
</tr>
</tbody>
</table>

Albumin was only measured once in plasma; it was 46 g/l 4.5 h after therapy began.

### Table 2. Response to the survey concerning the assessment of the ECF volume in this patient

<table>
<thead>
<tr>
<th>Estimated degree of ECF volume contraction</th>
<th>&lt; 20%</th>
<th>20–30%</th>
<th>&gt; 40%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of responses/total</td>
<td>21/98</td>
<td>61/98</td>
<td>16/98</td>
</tr>
<tr>
<td>Isotonic saline in the first hour (ml/kg)</td>
<td>&lt; 10</td>
<td>10–20</td>
<td>&gt; 20</td>
</tr>
<tr>
<td>Number of responses/total</td>
<td>10/98</td>
<td>65/98</td>
<td>23/98</td>
</tr>
</tbody>
</table>

The case synopsis and laboratory data were sent to 150 physicians and trainees. Approximately half of the 98 respondents were from paediatrics and the other half were from adult medicine. In both groups, we consulted endocrinologists, intensivists and nephrologists. Because there was no distinct pattern of response in any subgroup, the results were pooled and are reported for the whole group.
blood flow was probably not impaired sufficiently to merit aggressive saline administration (>10 ml/kg/h).

**Avoiding a fall in the effective P_{osm}**. The P_{Glu} will fall due to dilution (infused saline) and glucosuria when the GFR rises [6]. This will lower the effective P_{osm} unless the P_{Na} rises by a similar amount (about one-half the fall in P_{Glu}) [8]. To achieve this constant effective P_{osm}, the tonicity of the intravenous fluids should equal the P_{osm} during oliguria and the urine osmolality (U_{osm}) during polyuria [11]. Fortunately, the effective P_{osm} and U_{osm} are similar during a profound glucose-induced osmotic diuresis[12]. Luckily, the osmolality of isotonic saline plus 20–40 mM KCl is similar to this U_{osm}. Her effective P_{osm} on admission was 368 mOsm/kg H$_2$O and 12 h later it fell to only 359 mOsm/kg H$_2$O (P_{Glu} 27 mM and P_{Na} 166 mM). Later, the decline in P_{Na} should occur gradually to minimize rapid brain cell swelling.

**Teaching points**

(i) The magnitude of ECF volume contraction was best revealed by the haematocrit, while the response to therapy was reflected by the venous P_{CO$_2$} and the change in urine output.

(ii) The rate of saline infusion should be influenced by the urine output and the clinical assessment of the central nervous system status.

(iii) Hypotonic fluids should not be given because of the risk of cerebral oedema.

**Conflict of interest statement.** None declared.

**References**


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