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Nephrology
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Nephroquiz
(Section Editor: M. G. Zeier)

Seizures and renal failure: is there a link?

Case

A 70-year-old woman was referred to the emergency room of our hospital because of asthenia and polypnea. On physical examination, the patient was a slender woman who appeared to be afebrile and clinically hypovolaemic. Her vital signs were normal; there was no pedal oedema, blood pressure was 130/90 mmHg, and body weight 56 kg.

The levels of serum creatinine and urea nitrogen were 6 and 180 mg/dl, respectively, while sodium and potassium levels were 138 and 6.9 mmol/l, respectively. The levels of serum glucose and albumin were 110 and 3.6 mg/dl, respectively. Blood bicarbonate level was 13.5 mmol/l, pH 7.29 and $PaCO_2$ 30 mmHg. Haemoglobin value was 10 g/dl. An ultrasonographic examination of the abdominal area revealed kidneys markedly reduced in size without signs of urinary obstruction, and urine dipstick and microscopic examination were unremarkable.

A diagnosis of chronic renal failure probably due to nephrosclerosis coupled with metabolic acidosis partially compensated by respiratory alkalosis and hyperkalaemia in a well-nourished old patient was made. Intravenous therapy was started, composed of hydration treatment (isotonic saline and 5% dextrose with correction of the metabolic acidosis by 5% bicarbonate according to the formula: [(desired HCO_3 − observed HCO_3) × 30% body weight]. A few hours later, the old woman complained of aching upper limbs and suffered a bout of seizures.

Questions

What is the cause for the neuromuscular symptoms?
Is there a link between the intravenous therapy and neuromuscular symptoms of the patient?
What is your diagnosis?

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Answers to the quiz on the preceding page

Seizures due to hypocalcaemia worsened by shifting towards alkalosis by bicarbonate therapy.

Discussion

Calcium in the blood represents only 1% of total body content. The total plasma calcium concentration is 9–10 mg/dl (4.5–5.0 mEq/l = 2.25–2.50 mmol/l) and comprises a diffusible component (near 50%) mainly constituted of a freely ionized portion or a portion bound to other anions (phosphate, carbonate, citrate, lactate, sulfate), and one non-diffusable portion bound to proteins (mainly albumins) (Figure 1).

The biologically active component is the freely ionized portion, which is normally maintained within a tight range (1.0–1.25 mmol/l), depending on the concentration of plasma protein (mainly albumin), anion bound to ionized calcium, and blood pH. At a plasma pH of 7.4, each gram of albumin binds 0.8 mg/dl of calcium to its carboxyl groups. Hydrogen concentration strongly affects ionized calcium concentration, because both hydrogen ions and calcium are bound to albumin. Therefore, when acidosis is corrected to alkalosis, hydrogen ions are dissociated from albumin, allowing calcium to bind to albumin, further reducing the ionized calcium level; the contrary happens when acidosis occurs. Therefore, for each 0.1 increase in pH, ionized calcium decreases by about 0.05 mmol/l [1–3].

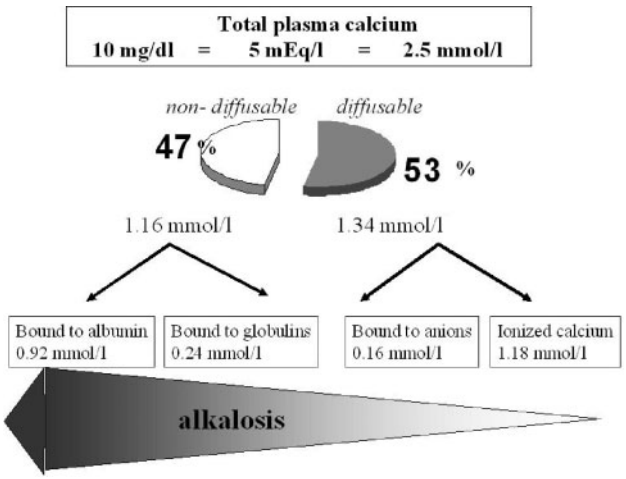

Fig. 1. Distribution of diffusible and non-diffusable calcium components in human plasma.

Furthermore, alkalosis affects the interaction between ionized calcium and the cell membrane by increasing myofibrillar calcium sensitivity [4,5].

Thus, when the ionized calcium concentration is even moderately decreased, alkalosis can precipitate tetany, and tetany can eventually occur even with a normal ionized calcium concentration in respiratory alkalosis [6–8].

Acute hypocalcaemia may present with clinical signs including tetany, carpopedal spasm and laryngeal stridor, cardiac dysrhythmias (prolongation of the QT interval), decreased cardiac contractility, hypotension and heart failure.

The above described patient had metabolic acidosis and hypocalcaemia due to chronic renal failure. Her calcium level was 6.0 mg/dl at baseline, but calcium replacement therapy was not adopted before bicarbonate therapy. A total of 235 mmol of sodium bicarbonate was calculated as supplementation therapy following the above mentioned formula $[(28 - 14) \times 16.5]$. Her tendency towards compensatory alkalosis (respiratory) was worsened by bicarbonate supplementation, eventually leading to a shift towards alkalosis. Therefore, her free ionized calcium concentration continued to decrease from the baseline value of 0.75 mmol/l to 0.65 mmol/l, and overt clinical symptoms of hypocalcaemia appeared (Table 1). The bicarbonate infusion was immediately replaced by one containing calcium gluconate up to regression of clinical symptoms.

In summary, free ionized calcium is the only portion physiologically active, and the balance between bound and unbound components is strongly influenced by changes to the blood pH, as any change towards

Table 1. Calcium and bicarbonate values before and after intravenous bicarbonate therapy without calcium supplementation

Serum parameters	Normal values	Time	
		Baseline	6 h after intravenous bicarbonate supplementation (235 mmol scheduled in 8 h)
pH	7.35–7.45	7.29	7.46
HCO_3	22–28 mmol/l	13.5 mmol/l	24 mmol/l
$paCO_2$	35–45 mmHg	30 mmHg	28 mmHg
Total calcium	9–10 mg/dl (= 4.5–5.0 mEq/l = 2.25–2.50 mmol/l)*	6 mg/dl (1.5 mmol/l)*	5.9 mg/dl (1.47 mmol/l)*
Ionized calcium	1.0–1.25 mmol/l	0.75 mmol/l	0.65 mmol/l
Albumin	3.5–5 mg/dl	3.6 mg/dl	–
Sodium	135–145 mmol/l	138 mmol/l	140 mmol/l
Potassium	3.5–5 mmol/l	6.9 mmol/l	5.8 mmol/l

*SI unit in brackets

alkalosis reduces the ionized (effective) component because it increases its attraction towards the protein bond.

Conflict of interest statement. None declared.

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