Reminder of important clinical lesson

Dyskalaemia following diffuse axonal injury: case report and review of the literature

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Summary

Traumatic brain injury, and its management, commonly causes derangements in potassium balance. There are a number of recognised causative factors including head trauma, hypothermia and iatrogenic factors such as pharmacological agents and permissive cooling. We describe a case of a 19-year-old man with a severe traumatic brain injury. In a 36-h period, his intracranial pressure increased despite maximal medical therapy and he developed refractory hypokalaemia. Immediately following a decompressive craniectomy, the patient was noted to be profoundly hyperkalaemic; this led to the development of ventricular tachycardia and cardiac arrest, from which the patient did not recover. The effects of brain injury on potassium balance are not well appreciated; the effect of decompressive craniectomy on potassium (K^+) balance has not been described previously. We would like to emphasise the potential effect of diffuse axonal injury, a severe form of brain injury and decompressive craniectomy on potassium balance.

BACKGROUND

Potassium imbalance occurs in the setting of traumatic brain injury and it may pose a challenge in an intensive care setting. We describe the first case of fatal dyskalaemia following decompressive craniectomy. We would like to stress the fact that potassium levels should be carefully monitored in patients with a brain injury, particularly in the setting of raised intracranial pressure (ICP). We suggest that permissive hypokalaemia in the absence of ECG changes be considered in this clinical setting with a low threshold for using haemofiltration to correct the abnormal serum potassium.

CASE PRESENTATION

A 19-year-old man fell from a galloping horse. The Glasgow Coma Scale (GCS) at the scene was 3/15. On arrival to hospital (a tertiary referral trauma centre) 1 h later, GCS was 7/15. Pupils were of normal diameter, equal and reactive to light. An initial CT brain, completed within an hour of arrival, was normal. There were no cervical or thoracic injuries. He was haemodynamically stable and his initial blood biochemistry tests were within normal limits. The patient's GCS improved to 9/15 over the course of a few hours and he was extubated. The patient's condition was stable for 24 h at which point his GCS dropped to 8/15. He was reintubated. An MRI brain, performed at that point, showed diffuse axonal injury (DAI; figures 1 and 2). A subsequent CT brain revealed interval development of cerebral oedema, with loss of grey-white differentiation in the cortex. An ICP monitor showed an initial reading of 15 mm Hg. This was stable until approximately 48 h later when, over a 12 h period, the patient had a simultaneous fall in serum potassium concentration ($[K^+]=2.3$ mmol/l) and increase in ICP (40 mm Hg). During the following 24 h the patient received maximal mannitol treatment (stopped when

serum sodium concentration=156 mmol/l), as well as appropriate increases in sedation and analgesia. His $PaCO_2$ was kept within normal limits. Despite intervention, the patient's ICP remained elevated; although 340 mmol of K^+ were infused in the 24-h period, his $[K^+]$ level dropped ($[K^+]=2.2$ mmol/l). Besides urine and gastrointestinal secretions, there were no fluid losses. Norepinephrine infusion was initiated to maintain a mean arterial pressure (MAP) ≥ 90 mm Hg and hence to maintain a cerebral perfusion pressure (CPP) ≥ 60 mm Hg (CPP=MAP-ICP).¹ Owing to persistent elevation of ICP and inability to maintain CPP, the patient underwent a decompressive craniectomy. The brain was found to be very oedematous intraoperatively.

Figure 1 Axial MRI fluid attenuated inversion recovery sequence demonstrating hyper intense bifrontal white matter abnormality.

Figure 2 Diffusion-weighted MRI axial image demonstrating signal change in corpus callosum and deep-left frontal white matter suggestive of diffuse axonal injury.

Shortly after returning to the intensive care unit, the patient's $[K^+]$ was noted to be 6.1 mmol/l. An ECG showed ventricular tachycardia. The patient was haemodynamically stable. The patient was given insulin, dextrose and calcium gluconate to manage the hyperkalaemia. Despite repeated infusions of insulin and dextrose, the $[K^+]$ levels rose to 6.5 mmol/l and an ECG showed broad complex tachycardia. There was no other significant change in the serum concentration of other electrolytes. When the patient became hypotensive, cardiopulmonary resuscitation (CPR) was started. Inotropic support did not improve the blood pressure. CPR was unsuccessful after 40 min, was discontinued and death was pronounced.

DIFFERENTIAL DIAGNOSIS

- ▶ Drug-induced dyskalaemia (suxamethonium, barbiturates and mannitol)
- ▶ Dyskalaemia following head injury
- ▶ Dyskalaemia secondary to hypothermia

DISCUSSION

Derangements in serum potassium concentration are common in the setting of brain injury. Box 1 summarises factors that predispose patients to dyskalaemia. We have classified these factors into extrinsic and intrinsic causes. Mild hypokalaemia is a feature of brain injury;²⁻³ it is attributed to a surge in catecholamines leading to β -2-adrenergic receptor stimulation and activation of the sodium-potassium pump, causing an intracellular K^+ shift.⁴ A strong correlation between $[K^+]$ and GCS (a guide to brain injury severity) has been demonstrated;⁵ in one study of 46 patients, the degree of hypokalaemia was found to be proportional to the fall in GCS. Exogenous inotropic support can augment the effect of endogenous catecholamines. Serum catecholamine concentration is related to ICP in the setting of brain injury and the relationship between the two is dynamically dependent on ICP.⁶⁻⁹ Studies have also shown that following head injury, there is an increase in cardiac output, blood pressure, pulse rate and pulmonary shunting along with

Box 1 Possible aetiological factors predisposing to dyskalaemia in brain injury

Extrinsic causes:

- ▶ Medication induced
 - Mannitol¹¹
 - Succinylcholine¹²
 - Barbiturates¹³
- ▶ Hypothermia¹⁷
- ▶ Predisposing medical conditions
 - Prolonged bed rest
 - Motor neuron disease
 - Skeletal muscle degenerative disease
- ▶ Postsurgical intervention-decompressive craniectomy (in our case)

Intrinsic causes:

- ▶ Traumatic brain injury causing secondary catecholamine surge³
- ▶ Increased intracranial pressure²⁻⁵

Idiopathic

decreased or normal systemic and pulmonary vascular resistance,¹⁰ consistent with increased circulating catecholamines. Insulin, known to cause hypokalaemia, has not been found to be elevated in patients with a traumatic brain injury.³ The same study found that changing insulin levels in patients with a brain injury had no impact on $[K^+]$.

Many aspects of neurointensive care and treatment are known to cause hypokalaemia. Mannitol has been shown to cause hypokalaemia when given in low dose and hyperkalaemia occurs in higher doses due to alteration in serum osmolality.¹¹ There are numerous reports describing dyskalaemia in patients who received suxamethonium (succinylcholine) secondary to increased expression of acetylcholine receptors on diseased muscle cells. Conditions predisposing patients to diseased-muscle cells include prolonged bed rest, motor neurone disease and skeletal muscle degenerative diseases. Depolarisation by suxamethonium releases K^+ from diseased muscle cells.¹² Barbiturates, long used as anaesthetic agents and as neuroprotective agents during neurosurgical procedures, have a known association with dyskalaemia.¹³⁻¹⁴ It is believed that this effect is mediated via several mechanisms including reversibly inhibiting voltage-dependent rectifier potassium channels and inhibition of intracellular phosphofructokinase.¹⁵ This leads to decreased production of the metabolic products pyruvate and lactate. A resultant increase in pH has the effect of initiating K^+/H^+ exchange such that H^+ ions move to the extracellular space and K^+ ions move into cells, leading to hypokalaemia. Barbiturates were not used at any stage in the care of our patient.

Iatrogenic hypothermia decreases the metabolic demands of the brain and is now commonly used in the management of traumatic brain injury. Hypothermia also causes hypokalaemia by at least two mechanisms: renal cell dysfunction and decreased ADH secretion leading to cold diuresis. Polyuria may deplete the body of all electrolytes, including potassium.¹⁶⁻¹⁷ It has been shown that hypokalaemia can be significant even with K^+ supplementation.¹⁸ Rewarming the patient reverses the loss of K^+ .

Given the incidence of traumatic brain injury, believed to be approximately 235/100 000 in Europe¹⁹ and 538/100 000 in North America,²⁰ and the close monitoring afforded to many of these patients, cases of symptomatic dyskalaemia are the exception, not the rule. In most cases, one or a combination of the factors described above is causative. There are few cases of symptomatic, biphasic dyskalaemia, where a cause is not apparent, such as that described in this case.^{21 22} In those previously reported cases, the use of K⁺-lowering agents and emergent, rescue haemofiltration were successfully used to control [K⁺].

Medical management failed to correct the raised ICP and hypokalaemia. Decompressive craniectomy corrected the ICP. It is possible that increased ICP may have triggered 'stress cardiomyopathy' secondary to catecholamine surge. This, and a sudden rise in [K⁺] to 6.1 mmol/l, may have precipitated the ventricular tachycardia.

To conclude, the combination of catecholamine surge along with the increase in ICP that preceded the decompressive craniectomy induced, in some unknown way, a massive shift of K⁺ to the intracellular space. The mechanism that caused the shift of K⁺ was reversed following surgery. The efflux of K⁺ was, in this case, fatal. As no other mechanism is obvious, we believe that β -2-adrenergic activity is the link between ICP and [K⁺]. One may argue that the inotropic support given to the patient may also have contributed to this phenomenon; however, the norepinephrine infusion was relatively constant during the event (both phases of the dyskalaemia) and is unlikely to have caused the biphasic dyskalaemia. We believe that the sudden fall in the serum potassium that coincided with the increment in ICP, and subsequent acute hyperkalaemia after the normalisation of ICP suggest that ICP and [K⁺] are linked.

Learning points

- ▶ Traumatic brain injury (diffuse axonal injury), by way of increased circulating catecholamines, can cause clinically significant dyskalaemia.
- ▶ Raised intracranial pressure may be the component, or one of many components, of traumatic brain injury that induce a catecholamine surge.
- ▶ We advise that potassium balance be carefully monitored in patients with traumatic brain injury, particularly in the setting of raised intracranial pressure.
- ▶ Although further research is required, we suggest that permissive hypokalaemia in the absence of ECG changes be considered.
- ▶ When decompressive surgery is indicated, intraoperative and postoperative changes in serum potassium concentration should be managed immediately. There should be a low threshold for using haemofiltration to correct hyperkalaemia.

Competing interests None.

Patient consent Obtained.

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