Iraq: the environmental challenge to HM Land Forces

Michael J World and Thomas C Booth

ABSTRACT – In 2003, occasional military patients with hyponatraemia, hypokalaemia and alkalosis were encountered in Iraq. Development of central pontine myelinolysis in one patient indicated treatment should be cautious. Two years later, heat illness continued to occur during the very hot summer months and 23 cases were admitted to a British military field hospital near Basra, Iraq. Incidence was <0.15% of deployed personnel per summer month. Serum sodium and potassium concentrations were directly (r=0.66, p=0.0002) and serum sodium and bicarbonate concentrations inversely (r=–0.64, p=0.002) correlated. The magnitude of these changes was unrelated to the glomerular filtered load of sodium. While blood pressure was undiminished, estimated glomerular filtration rate was reduced. These electrolyte changes were compatible with secondary hyperaldosteronism but field conditions constrained further investigation. Hyponatraemia was probably due to salt deficiency rather than overhydration. In some military personnel summer salt supplementation could be essential during operations in hot countries.

KEY WORDS: alkalosis, heat illness, hyponatraemia, salt supplementation, secondary hyperaldosteronism

Introduction

Definition of heat illness

Heat illness with raised core temperature causes variable ataxia and impairment of consciousness in a previously fit individual. High environmental temperature and humidity were correlated with increased incidence of this condition in British military personnel in India a century ago.[1] More recently cases have occurred in Iraq and Afghanistan. An internal audit showed that in Iraq between March and September 2003, 849 cases of heat illness occurred. Causative factors were assessed in 545 of these and 11 considered likely but hyponatraemia was not included.

History of prophylactic use of salt tablets

Tropical use of salt tablets by British forces in times past is legendary. A contemporary reference to the initiation of this prophylaxis has been elusive. The evidence suggests this first occurred sometime during the second world war.[2–4] Despite awareness of morbidity and mortality in hot climates, the classic studies of salt deficiency by McCance before this war make no mention of dietary salt supplementation by the military as a prophylaxis for heat illness.[6–8] McCance commented that in the absence of inactive storage capacity for sodium, a constant supply was important.[9] Periods of deficiency could be survived if excretion was minimised but large amounts of salt were required if excretion increased as occurred in workers in hot environments.[9,10] Prophylactic salt administration may have been considered but McCance made no reference to this.

Prophylaxis in the present campaign

When medical planning for the present campaign in Iraq was undertaken advice about adequate water intake was emphasised but salt supplementation was not. Such action was considered unnecessary if salt conservation by the kidneys was adequate when the environmental challenge was limited artificially. This article examines the wisdom of this decision.

Methods

Patients presenting with apparent heat illness were examined in routine fashion. Venous blood was drawn in the usual way. Serum urea, creatinine, sodium and potassium concentrations were measured by dry-state technology using an Ortho-Vitros DT60® analyser. Serum bicarbonate was measured using an Abbott i-STAT® portable clinical analyser. Both manufacturers provided standard samples for control purposes.

Herald cases

Case 1

A 27-year-old Private in the territorial army (TA) presented on 5 April 2003 at the military field hospital close to Basra feeling unwell despite consuming six litres of water daily, which was appropriate given midday temperatures of 42°C. Table 1 shows observations in Basra and after almost three months back in UK. A relative defect in sodium absorption in the

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proximal nephron resulting in secondary hyperaldosteronism as described in Bartter's syndrome and other hypokalaemic salt-losing tubulopathies was possible.[11] Spontaneous recovery occurred on return to the temperate UK. Three 24-hour urine collections showed normal renal function (mean creatinine clearance=111 ml/min (range 86–129)), normal fractional excretion of sodium (0.5% (0.1–0.9)) and potassium (9.3% (7–13)) and normal free water clearance of –1396 ml (–1082 to –2019).

Case 2

A 36-year-old Corporal in the TA was admitted on 8 July 2003 to the same field hospital with a one-week history of shortness of breath and vomiting. Peripheral haemoglobin oxygen saturation (SpO_2) remained depressed at 78–85% despite 15 l/min supplemental oxygen. He was found to have a right lower lobe pneumonia. Blood pressure was 105/60. Blood urea was 13.9 with plasma sodium 99 and potassium 1.5 mm/l. Arterial blood gas results were unavailable. He was intubated, ventilated and given intravenous (iv) normal saline with potassium supplements and antibiotics. Two days later (10 July 2003), he was extubated and the following morning, plasma sodium was 131 and potassium 4.0 mm/l. A day later (12 July 2003) he felt unwell, had a persistent flattened affect and an unsteady gait. He arrived in Birmingham on 17 July 2003. Before investigation, he absconded to his home over 100 miles away. Friends found him to be unwell and took him to a local hospital. Hallucinations and other neurological abnormalities were noted. A magnetic resonance brain scan showed central myelinolysis, mainly pontine but affecting extrapontine cerebral white matter as well (Fig 1). After psychiatric treatment for hallucinations, he was admitted to a defence rehabilitation unit. Recovery sufficient for continued military service followed two months' treatment for minor residual neurological problems.

Table 1. Clinical and laboratory data on herald case 1.

Date	5 April 2003	9 April 2003	29 June 2003
Location	**Basra, Iraq**	**Basra, Iraq**	**Birmingham, UK**
Blood pressure, lying (mmHg)	116/63	–	102/48
Blood pressure, standing (mmHg)	116/73	–	106/73
Blood urea (mm/l)	7.2	7.2	5.0
Creatinine (μm/l)	106	98	99
Na (mm/l)	111	132	142
K (mm/l)	2.4	2.7	4.4
Arterial pH	7.62	7.72	7.46
$PaCO_2$ (mmHg)	29	24	41
HCO_3 (mm/l)	29	33	25

Heat illness cases, June-August 2005

Twenty-three cases of heat illness (<0.15% of deployed personnel per summer month; 30% of medical admissions) were admitted to the same field hospital over the two months from mid-June to mid-August 2005. Median serum sodium was reduced at 130 mm/l (interquartile range=122.5–137). The median mean arterial pressure (MAP) was 96.4 mmHg (86.3–102.3). Glomerular filtration rate (eGFR) was estimated by the Cockcroft–Gault equation and median value was 79 ml/min (62–95). Cases with more severe hyponatraemia had more severe hypokalaemia and higher serum bicarbonate concentrations. Statistical testing for linear correlation

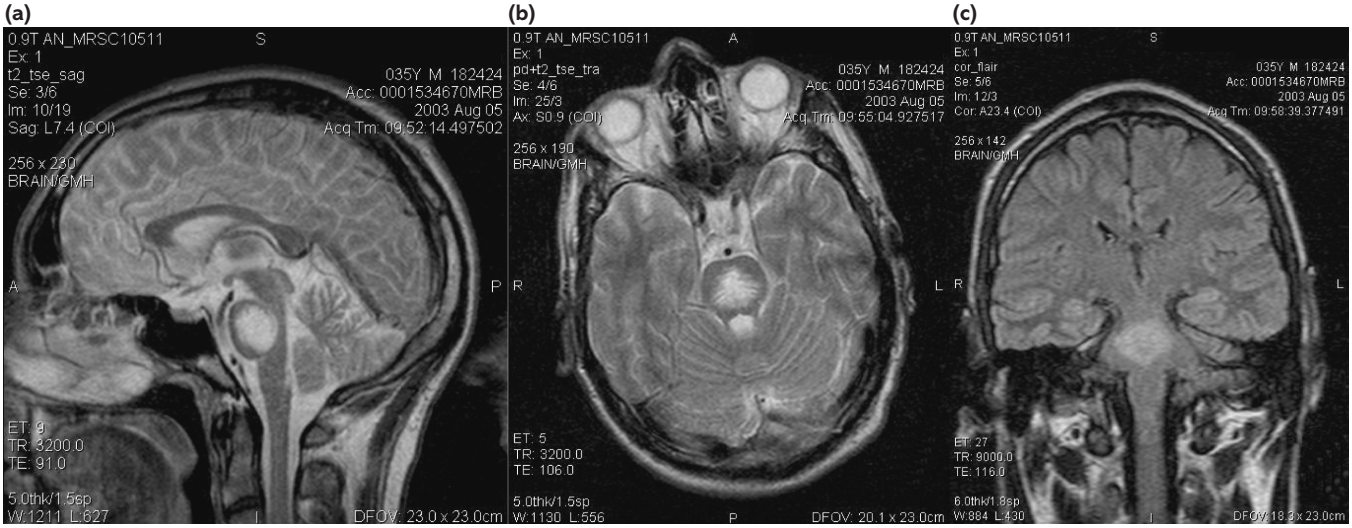

Fig 1. Magnetic resonance brain scan showing features compatible with central myelinolysis, mainly in the pons but also in extrapontine white matter on median (a), midbrain transverse (b) and midbrain coronal (c) sections. Reproduced with permission of Dr Hoadley FRCR.

showed sodium concentration directly correlated with serum potassium (r=0.66, p=0.0002) and inversely correlated with serum bicarbonate concentration (r=-0.64, p=0.002) (Fig 2).

Relationship between serum sodium, eGFR and MAP

To determine factors that could have contributed to the hyponatraemia, correlations were sought between:

- serum sodium and MAP (r=0.47, p=0.4)
- serum sodium and eGFR (r=0.31, p=0.15).

In both cases, inverse correlations were expected if overhydration was contributory. However, the results showed statistically insignificant trends whose nature was the reverse of that expected if overhydration was a factor.

Confirmation of secondary hyperaldosteronism was not possible

Hyponatraemia combined with hypokalaemia and elevated bicarbonate concentration suggested the presence of secondary hyperaldosteronism. Unfortunately, there was no facility to measure urinary sodium or potassium, serum renin, aldosterone or arginine vasopressin levels.

Estimation of activation of sodium absorption by the distal nephron and its relationship with increasing glomerular filtered load of sodium

In order to assess the degree of activation of sodium reabsorption by the distal nephron in each case, the magnitude (mm/l) that serum potassium was depressed below 5 mm/l was added to the magnitude (mm/l) that serum bicarbonate was elevated above 20 mm/l and the resultant sum was termed, for the sake of argument, the distal convoluted tubule (DCT) activity index. There was a statistically significant inverse correlation between the latter and serum sodium concentration (r=-0.65, p=0.0013, Fig 2). If there was a defect in proximal nephron sodium absorption, an increase in DCT activity index might be expected with increasing glomerular filtered load of sodium (GFL-Na, mm/min), calculated by multiplying serum sodium concentration (mm/ml) by eGFR (ml/min) in each case. Instead of a statistically significant direct correlation, an inverse trend (r=-0.23, p=0.33) was found. Although eGFR was the major determinant of GFL-Na (r^2=0.97, unlike serum (Na) where r^2=0.22), there was no significant correlation with DCT activity index (r=-0.12, p=0.61).

Case controls

An institutional review board consisting of non-clinicians (medical support officers, padre and welfare workers) approved examination of case controls, subject to informed consent. Thereafter patients were asked if there was a colleague of same sex and approximately same weight in the same unit who had been employed on the same task at the time of illness who had remained unaffected who might act as a control. Ten such pairs were studied. There was a trend towards lower serum sodium concentrations in cases (mean Na (± SD)=129 (10.4)) when compared by Student's t test for matched pairs with controls (137 (4.8)) but the difference was not statistically significant (t=1.8, p=0.1).

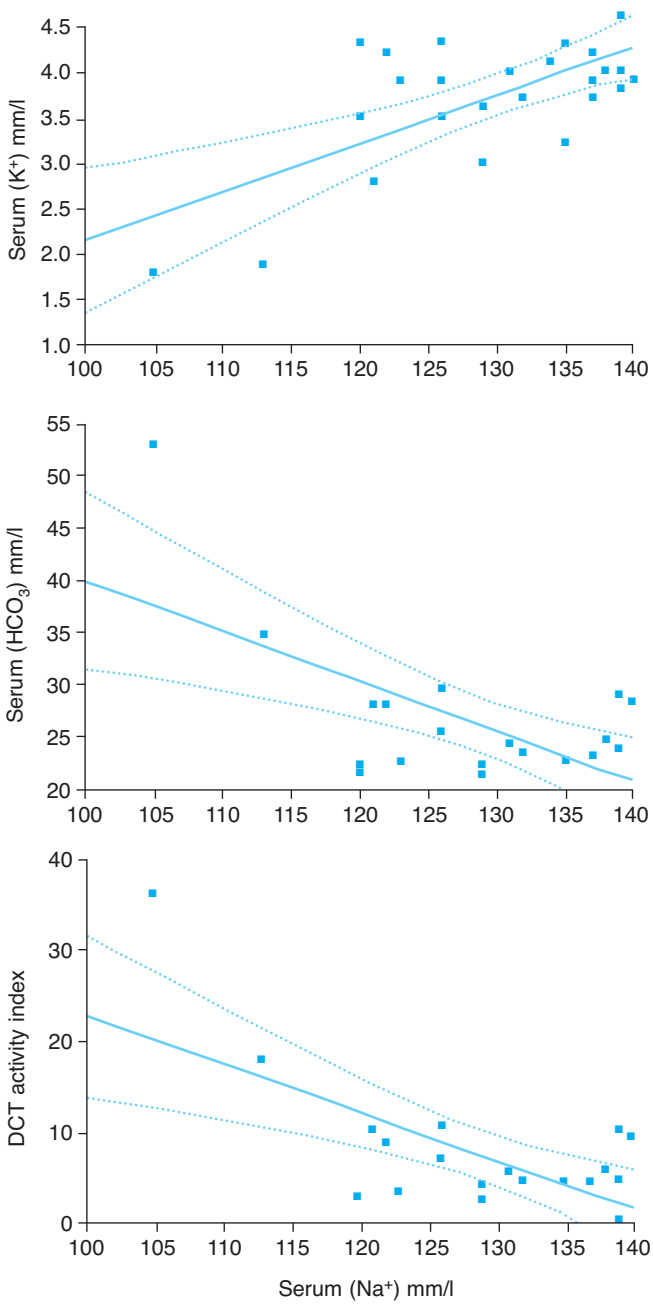

Fig 2. Graphs (regression lines with 95% confidence limits) showing relationships between (upper) serum sodium concentration (Na) and serum potassium concentration (K) (r=0.66, p=0.0002), (middle) serum sodium concentration (Na) and serum bicarbonate concentration (HCO_3) (r=-0.64, p=0.002), (lower) serum sodium concentration (Na) and distal convoluted tubule (DCT) activity index (see text for explanation: r=-0.65, p=0.0013).

Discussion

Low risk of hyponatraemic heat illness

Some 8,500 British soldiers were deployed at the time that the cases of heat illness were admitted, less than 0.15% of the population at risk per summer month. None of the patients took diuretics which could have lowered the threshold for this problem.

Potential for dilutional hyponatraemia

Sodium concentration in sweat varies from 25 mm/l in normal individuals to 50–70 mm/l in the unacclimatised or those with cystic fibrosis.[12,13] In the absence of other compensations, isovolumetric replacement of sweat by ingested water can result in marked hyponatraemia. For example, in an individual with a serum (and hence extracellular fluid (ECF)) sodium concentration of 140 mm/l, a six-litre sweat loss will incur a salt deficit of at least 150 mm from a total ECF content of about 1,960 mm leaving 1,810 mm. Maintenance of normal ECF volume at 14 litres with water will lower serum sodium concentration to 129 mm/l. In Iraq, bottled water is stacked on pallets for consumption by soldiers as required. This raises the possibility that overhydration could contribute to hyponatraemia with cerebral disturbance as has been seen in marathon runners.[14,15]

Renal function and hormonal profile in marathon runners

Endurance athletes (marathon and double-marathon runners) have normal or increased urine output and creatinine clearance while fractional sodium excretion is reduced.[16,17] This enhanced renal function would be compatible with overhydration status and is maintained even when hyponatraemia is associated with relatively reduced plasma volume, increased serum renin and aldosterone concentrations.[17,18] In triathletes, serum arginine vasopressin concentration was appropriately depressed in overhydrated hyponatraemic subjects.[19] Such endocrine studies were impossible in the field hospital.

Renal function in the military patients

The observation that the military cases tended to have depressed eGFR makes overhydration unlikely. Moreover, the Cockcroft–Gault equation employed to calculate eGFR tends to overestimate GFR when compared with more accurate methods which adds confidence that the lowered eGFR found in military patients really is depressed.[20–23] These findings are similar to those described by McCance in experimental salt deficiency where plasma volume fell causing haemoconcentration (haemoglobin concentration rose 26%) and an elevation (circa 4%) of total protein concentration.[6–8] Blood pressure was maintained but azotaemia and a fall in creatinine clearance of 30% were noted.

Hyponatraemia alone triggers sodium retention by the distal nephron

The lack of a direct correlation between the DCT activity index and GFL-Na suggests that in these patients, there is no graded increase in aldosterone secretion as GFL-Na rises. The ability of the proximal nephron to reabsorb adequate amounts of sodium to compensate for sweat losses has already been exceeded and with falling serum sodium concentration, the distal nephron is activated to enhance sodium reabsorption.

Minimising the risk of central pontine myelinolysis

Speedy *et al* discussed the risks of precipitating central pontine myelinolysis (CPM) by too rapid correction of hyponatraemia.[14] Careful correction of serum sodium concentration generally relieved the encephalopathy associated with hyponatraemia without this complication. Confining the present patients to a cooler environment resulted in rapid recovery with resumption of spontaneous unforced consumption of oral fluids after modest amounts of iv physiological saline with supplemental potassium. Gradual resolution of hyponatraemia occurred without the need for other measures such as potentially more hazardous administration of hypertonic saline.[24]

Experimental salt prophylaxis

Taylor *et al* showed that moderate daily salt intake (14.7 g) lowered pulse rates in both soldiers and students subjected to periods of dry heat lasting 84 and 48 hours respectively.[25] Tilt table studies showed reduced postural hypotension and reflex tachycardia. Plasma chloride concentration was maintained and rise in blood urea seen on a low salt diet (5.8 g daily) reduced. Finally, analysis of the data of Taylor *et al* using Fisher's exact test showed that moderate salt diet reduced the prevalence of prostration from 25% to less than 3% ($p=0.013$).

Beneficial effects of salt administration in tropical heat illness

MacLean described the successful treatment of an epidemic of 14 cases of tropical heat illness over four days in June 1943 on board a warship.[26] The patients received oral saline. Prophylactic oral saline providing 20–30 g salt daily reduced the frequency of heat illness to less than one case monthly over the next seven months.

Hubbard and Armstrong suggested that salt supplementation was not necessary in hot climates as Bedouin tribesmen and other natives of hot countries did not require this.[27] Unlike such well-adapted natives, some soldiers deployed from temperate countries may lack adequate renal reserve capacity to conserve sodium and compensate for sodium loss in sweat, and develop hyponatraemia with its adverse cerebral effects. Maintenance of their operational capability and their welfare needs consideration.

Factors contributing to cerebral impairment in heat illness

In cases of heat illness, several factors might contribute to impairment of cerebral function apart from elevated core temperature. Hyponatraemia is one such factor and could arise due to water

intoxication mentioned previously or inadequate renal salt conservation or both. In the cases presented here, water intoxication cannot be completely excluded. However, apart from the desert environment, there is much evidence to suggest this was not the major factor. Plasma urea and creatinine were relatively elevated at the time of presentation in the herald cases. Serum bicarbonate concentrations were elevated rather than depressed. Any relationship between serum sodium and eGFR was the reverse of that expected if overhydration was contributory and eGFR (Cockcroft–Gault) was depressed.

Salt prophylaxis

Should salt supplementation be recommended for current military operations in the Middle East? It probably should but not necessarily as tablets. A distinction needs to be made between the deleterious effects of chronic excess salt consumption in temperate locations and the preservation of body salt levels in tropical areas by regularly taking moderate amounts of salt with food.

Potential civilian impact of global warming

These findings could be relevant to civilians living in temperate places that are potentially subject to the effects of global warming. During an exceptionally hot July in 2006 in Birmingham, a previously fit young adult civilian patient who was not taking diuretics was admitted with impaired consciousness necessitating intubation and ventilation. Hyponatraemia, hypokalaemia, alkalosis and reduced predicted GFR with markedly raised serum renin and aldosterone were found. Cautious correction of these electrolyte disturbances eventually restored the patient to good health. This case will be the subject of a subsequent report.

Statement of contributions

The project was initiated jointly. TB collected much of the clinical data. MW analysed the results, wrote the paper including the introduction, the summary of published work, the discussion and conclusions.

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