

# Dietary Supplements and Military Operations: Caution is Advised

CJ Boos<sup>1,2,3</sup>, SH White<sup>2</sup>, SA Bland<sup>1</sup>, PD McAllister<sup>4</sup>

<sup>1</sup>MDHU(Portsmouth), Queen Alexandra Hospital, Cosham PO6 3LY, <sup>2</sup>Hospital Squadron, UK Medical Group, British Medical Hospital, Basrah, Op Telic, BFPO 641; <sup>3</sup>Poole Hospital NHS Trust, Poole, Dorset, BH15 2JB; <sup>4</sup>CA Psych (Army), DCMH Tidworth, Wilts, SP9 7EA

## Abstract

We describe the case of a 32-year-old soldier who presented with acute organic psychosis during an operational tour to Iraq. This was precipitated by excessive consumption of caffeine coupled with additional use of oral nutritional stimulants. Her biochemical profile was compounded by the additional use of exogenous creatine. We present a brief overview of the issue of exercise supplementation and highlight some of the potential problems and clinical issues surrounding their use. This has important implications for both serving soldiers and the wider medical community.

## Case report

A 32-year old soldier was admitted to the Emergency Department with an acute confusional state. She was three weeks into her first operational tour to Iraq on Op TELIC 13. She had an unremarkable past medical and psychiatric history, with the exception of a minor antecedent frontal head injury six weeks previously. Her father had suffered with a major depressive episode following his separation from the patient's mother. The patient was a non-smoker and had a previous history of heavy alcohol consumption of up to 60 units/week prior to deployment. She denied taking any regular medications.

She had complained of a two day history of insomnia with approximately six hours total sleep over the previous two nights. On the day of admission she had become increasingly unwell over the course of the morning and had voluntarily missed breakfast. At approximately 1100 hours, on the day of admission, she had complained of feeling sweaty, flushed, clammy, tremulous and increasingly irritable. She avoided lunch and went to her bed to lie down at 1300 hours. At 1800 hours she was awoken by her colleagues who had become concerned of her whereabouts. She was noted to be flushed, sweaty and clammy. Witness reports suggest that the patient was noticeably dysarthric, agitated, incoherent and displayed extreme paranoia. At the time of arrival in the Emergency Department she was noted to be sweaty, clammy, flushed, agitated and was hallucinating and described seeing 'three men dressed in black' at the end of her hospital trolley. The patient had no memory from 1400 to 1900 hours on the day of admission.

On examination she was apyrexial with a heart rate of 78/minute and a blood pressure of 118/70 mmHg with oxygen saturations of 98% on air. On examination she was clinically flushed with a fine resting tremor. She was hyperreflexic with mild persistent nystagmus, both of which slowly improved. There was no rash, focal neurology or photophobia and no evidence of alcohol intoxication.

She was initially commenced on intravenous acyclovir and ceftriaxone for a possible diagnosis of meningitis/encephalitis. Her symptoms slowly abated over two hours with recovery of full mental function. Her initial full blood count (including mean cellular volume), liver function tests (including gamma GT), creatinine kinase, fasting blood glucose (4.2 mmol/L), urine dipstick and pregnancy test, erythrocyte sedimentation rate and C reactive protein were all normal. Arterial blood gases were also normal with no features of hyperventilation and normal blood lactate levels. However, her serum creatinine was elevated at 136 µmol/L (normal 62-106), with normal sodium (142 mmol/L) potassium (4.2 mmol/L) and urea (2.4 mmol/L). There was a significant difference between her measured (339 mosm) and calculated serum (285.00 mosm) osmolality of 54 mosm in keeping with an increased (>10 mosm) osmolar gap. She underwent a CT scan of her head, to exclude a space occupying lesion or subdural haematoma, which was unremarkable. In view of her rapid improvement coupled with unremarkable inflammatory markers, her acyclovir and ceftriaxone were discontinued after one dose as it was felt that either meningitis or encephalitis were unlikely diagnoses.

On further questioning, the patient had admitted to taking creatine supplements (Creatamax) over the previous three weeks (one tablet twice daily). She had also commenced the stimulant Ripped Fuel™ Ephedra Free (Twinlab Laboratories, Inc, Ronkonkoma, NY) at an increased initial dose of two tablets three times daily 48 hours prior to admission (Figure 1). Furthermore, she confessed to drinking six cans of Red Bull and six cups of strong coffee per day, including four of each on the day of admission. Her subsequent serum creatinine level (82 µmol/L), which was taken the following morning post admission (when her creatine supplements had been stopped for a two further doses) had returned to normal in the absence of intravenous rehydration. She was assessed by the Field Mental Health Team and was medically discharged back to her unit, within 24 hours of her admission with a diagnosis of a possible acute psychotic reaction secondary to the combination of excess caffeine intake and use of stimulants. She was stopped from carrying weapons until a further 48 hours later. Her repeat measured osmolality (289 mosm) and osmolar gap

Corresponding Author: Christopher Boos, Department of Cardiology, Poole Hospital, Longfleet road, Poole, Dorset, BH15 2JB

Email: Christopherboos@hotmail.com

(<10 mosm) at 72 hours post admission had returned to normal. Subsequently, her urine toxicology screen (reference laboratory in the UK), blood alcohol level and thyroid function levels from the time of admission were all normal. The patient, who had always admitted a desire to stay on tour, was discharged back to her unit in theatre.

## Discussion

We present a case of an acute organic psychotic reaction or conversion illness secondary to excessive caffeine intake coupled with insomnia and stimulant use. This case raises a number of important clinical issues related to the use of exercise and dietary supplements among deployed military personnel.

The use of supplements to potentially augment exercise performance is a multi billion dollar industry worldwide and continues to expand. The spectrum of products included in this umbrella term is vast and includes stimulants (such as caffeine and synephrine), protein supplements, creatine, anabolic steroids, carbohydrates, minerals and vitamins[1]. The use of exercise supplements has been previously investigated amongst American military personnel and has increased from 35% reporting daily use in one study in 1991 to 76% in a more recent cohort in 2003[2]. However, there have been no studies in the British Military to date. This is important as whilst the majority of supplements are known to be relatively safe, there are essential caveats that must be appreciated which include questions over product purity, efficacy, lack of robust research evidence to support their use and the potential for interactions/synergy with other agents. Our patient had bought her supplements from her local NAAFI in Germany, but a number of unlicensed internet sources have been cited in recent years.

Creatine is one of the most widely used exercise supplements today[3]. It became commercially available in 1993, after the 1992 Olympics when Linford Christie and other athletes admitted to using them. It is taken to help increase muscle size and power and appears to have some small benefit in anaerobic muscle activity for short explosive periods and may have therapeutic uses.

Exogenous creatine supplementation leads to increased intramuscular and cerebral stores of creatine and its phosphorylated form, phosphocreatine. The increase of these stores can offer benefits to the athlete by preventing ATP depletion, stimulating protein synthesis or reducing protein degradation, and stabilizing biological membranes. Creatine supplementation can lead to increasing muscular force and power, reducing fatigue in repeated bout activities, and increasing muscle mass[3,4]. It may also have potential therapeutic benefits in a host of neurological diseases such as Huntington's, Parkinson's and Duchenne muscular dystrophy with no convincing evidence of significant side effects[5].

Creatine is osmotically active and increases intracellular and total body water leading to weight gain[3]. Oral creatine is converted to creatinine in the body and can lead to increased circulating creatinine levels, without true impairment in renal function[6,7]. The observed rise in serum creatinine is usually very mild (<30%). However, the effects have been shown to be accentuated with

fasting, as in our case[4]. This might explain the increased osmolar gap noted in our patient, which has itself been previously described with creatine use[5,7]. Awareness of supplement use is vital for military clinicians especially in the context of treating patients with heat illness.

Stimulants are frequently used as an exercise aid to improve exercise motivation, duration of training and to augment weight loss. The stimulant herb ephedra was previously one of the most commonly used stimulants until 2004 when it was removed from the market owing to an increasing number of serious cardiac and psychiatric related side effects. Consequently, dietary supplement manufacturers have replaced ephedra with a number of alternative stimulants. In a recent survey of 36 products marketed as ephedra-free, 32 (89%) contained a methylxanthine such as caffeine or theobromine, 21 (58%) contained the stimulant synephrine, and 20 (56%) contained both a methylxanthine and synephrine[8].

Ripped Fuel™ ephedra free contains three main ingredients: bitter orange/Citrus aurantium 325mg (6% synephrine, a sympathomimetic alkaloid), Guarana seed extract (22% caffeine) and St John's Wort extract. Hence, whilst these products may be ephedra-free they certainly are not necessarily stimulant-free or risk-free and have been linked to an increasing number of reported adverse effects[9-16]. These adverse effects are thought to be attributable to the combination of caffeine and other stimulants in the multi-component formulation[17]. Synephrine is one of the adrenergic amines that stimulates the beta-3 receptors with minimal impact on the other receptor sites. This functions to increase the metabolic rate without affecting heart rate or blood pressure. Synephrine releases adrenaline and noradrenaline only at the beta (B)-3 receptor sites (mostly adipose tissue and the liver). Stimulation of the B-3 receptor sites elicits lipolysis[17]. The warning on the packaging states that it should be avoided in patients with psychiatric disease, nervousness and anxiety, depression or seizure disorders.

Caffeine itself is a widely used stimulant and has been linked to a number of psychiatric symptoms[18]. For example, it can cause anxiety symptoms in normal individuals but particularly in vulnerable patients with pre-existing anxiety disorders. Caffeine use has also been associated with symptoms of depression, insomnia and changes in mood. Psychosis has been induced in normal individuals ingesting toxic doses and it has been linked to worsening of psychotic symptoms in schizophrenic patients[18]. The combination of caffeine in coffee, Red Bull™ and Ripped Fuel™ ephedra free combined with the additional stimulants of synephrine and St John's Wort, in our patient, is excessive and appears more than coincidental and was the likely cause of the patient's insomnia, anxiety and perhaps delirium.

In summary, we present a case of apparent delirium that may have been precipitated by heavy concomitant use of caffeinated drinks in combination with the supplement Ripped Fuel™. This has potential implications for the wider military and suggests a need for an increased awareness by both clinicians and the military to prevent and treat potential unwanted side effects related to their use. A cross sectional study on their use amongst the British Military is needed.

## References

- Ahrendt DM Ergogenic aids: counseling the athlete. *Am Fam Physician* 2001;63:913-22.
- Bovill ME, Tharion WJ, Lieberman HR. Nutrition knowledge and supplement use among elite U.S. army soldiers. *Mil Med* 2003;168:997-1000.
- V J Dalbo, M D Roberts, J R Stout, C M Kerksick. Putting to rest the myth of creatine supplementation leading to muscle cramps and dehydration. *Br J Sports Med*. 2008;42:567-73.
- Kreider RB. Effects of creatine supplementation on performance and training adaptations 2003 ;244:89-94.
- Watson G, Casa DJ, Fiala KA, et al. Creatine use and exercise heat tolerance in dehydrated men. *J Athl Train* 2006;41:18-29.
- Pline KA, Smith CL. The effect of creatine intake on renal function. *Ann Pharmacother*. 2005;39:1093-6.



Figure 1. Container of Ripped Fuel™ Ephedra free used by the patient.

7. Persky AM, Rawson ES. Safety of creatine supplementation. *Subcell Biochem.* 2007;46:275-89.
8. Gregory PJ. Evaluation of the stimulant content of dietary supplements marketed as "ephedra-free". *J Herb Pharmacother.* 2007;7:65-72.
9. Haller CA, Benowitz NL, Jacob P 3rd. Hemodynamic effects of ephedra-free weight-loss supplements in humans. *Am J Med* 2005;118:998-1003
10. Marcus DM, Grollman AP. Ephedra-free is not danger-free. *Science* 2003;301:1669-71.
11. Burke J, Seda G, Allen D, Knee TS. A case of severe exercise-induced rhabdomyolysis associated with a weight-loss dietary supplement. *Mil Med* 2007;172:656-8.
12. Willis SL, Moawad FJ, Hartzell JD, Iglesias M, Jackson WL. Hypertensive retinopathy associated with use of the ephedra-free weight-loss herbal supplement Hydroxycut. *MedGenMed* 2006;8:82.
13. Holmes RO Jr, Tavee J. Vasospasm and stroke attributable to ephedra-free xenadrine: case report. *Mil Med* 2008;173:708-10.
14. Nasir JM, Durning SJ, Ferguson M, Barold HS, Haigney MC. Exercised-induced syncope associated with QT prolongation and ephedra-free Xenadrine. *Mayo Clinic Proceedings* 2004;79:1059-62.
15. Bent S, Padula A, Neuhaus J. Safety and efficacy of citrus aurantium for weight loss *Am J Cardiol* 2004;94:1359-61.
16. Jordan S, Murty M, Pilon K. Products containing bitter orange or synephrine: suspected cardiovascular adverse reactions. *CMAJ* 2004;171:993-4.
17. Colker CM, et al. Effects of citrus aurantium extract, caffeine, and St. John's Wort on body fat loss, lipid levels, and mood states in overweight healthy adults. *Current Therapeutic Research* 1999; 60: 145-153.
18. Broderick P, Benjamin AB. Caffeine and psychiatric symptoms: a review. *J Okla State Med Assoc* 2004;97:538-42.