Reminder of important clinical lesson

Running a risk? Sport supplement toxicity with ephedrine in an amateur marathon runner, with subsequent rhabdomyolysis

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Summary

A 36-year-old man presented to the emergency department acutely unwell after being found collapsed while running a halfmarathon. He presented with a reduced Glasgow coma score, was tachycardic, agitated, hypoxic and profusely sweating. He had taken a 'supplement' given to him prior to the race by a friend, as he was concerned about not finishing. This contained both caffeine and a large dose of ephedrine (60 mg in total). After initial resuscitation he was intubated, and was transferred to critical care. He subsequently developed rhabdomyolysis, requiring haemofiltration.

BACKGROUND

This case demonstrated some important learning points, and is a recognised but uncommon presentation. It highlights the dangers of taking supplements from unreliable sources, and the ease in which they are obtained. It is also not something just taken by elite athletes; amateurs are also taking supplements to aid performance. Consumers do often not know the contents of these, or their actions. Therefore many patients may use supplements, with possible significant health consequences. When sporting events are taking place, it is important that medical staff are vigilant as to the possibility of toxicity from these drugs, when patients present apparently just 'collapsed due to exhaustion'. Also, if a supplement is implicated, then its contribution to potential future complications needs to be recognised.

CASE PRESENTATION

The patient was brought into the emergency department by ambulance, after having an unwitnessed collapse towards the end of his half-marathon run. On arrival, he had a Glasgow coma score (GCS) fluctuating between 12 and 13, was hypoxic, and profusely sweating with a temperature of 39°C. He was also very tachycardic (heart rate 142), and had grossly dilated pupils bilaterally. He was initially resuscitated, before becoming hypoglycaemic and later having two seizures. He was then intubated, and taken to the CT scanner, before being transferred to the critical care unit. When his family arrived we were told he was previously fit and well, and his friend had given him a 'pill' before starting the race, as he was concerned about finishing in a good time. The label identified the tablet as containing ephedrine 30 mg, as well as aspirin 30 mg, caffeine 120 mg and narnegin 80 mg – he had taken two of these. He had also had a recent chest infection.

INVESTIGATIONS

When found by paramedics, his saturations were 78% on air, increasing to 92% on 15 litres of oxygen via a non-rebreather mask. His heart rate was 142 and blood pressure

110/60 mm Hg. His full blood count and coagulation screen was relatively normal, but urea and electrolytes showed a potassium level of 6.2 mmol/l, creatinine of 188 µmol/l and urea of 7.6 mmol/l. His creatine kinase (CK) was also 2975 U/l. ECG showed a sinus tachycardia, as well as a S1 Q3 T3 pattern. His initial arterial blood gas showed a metabolic acidosis with a lactate of 14.7 mmol/l.

DIFFERENTIAL DIAGNOSIS

Initial thoughts were drug toxicity, possibly with amphetamines. Due to his hypoxia we also wanted to exclude a pulmonary embolism, as well as intracranial pathology due to his decreased GCS and seizures.

TREATMENT

He was initially given high flow oxygen, intravenous fluids, cooled with a fan and sponging, and given dextrose/insulin infusion and calcium gluconate. A toxicology screen was sent.

OUTCOME AND FOLLOW-UP

His blood sugar dropped on several occasions, requiring a dextrose infusion, and he also suffered two seizures while in the resuscitation room. He was subsequently intubated, and taken to the CT scanner. His CT head was reported as normal, with a CT pulmonary angiogram showing only some possible right lower lobe consolidation. He was transferred to critical care for further management. While in critical care he required haemofiltration for acute renal failure secondary to rhabdomyolysis. His initial CK of 2975 U/l on admission peaked at 130 098 U/l. He required a week of continuous veno-venous haemofiltration and subsequently haemodiafiltration before being discharged from critical care and having further intermittent renal replacement therapy.

DISCUSSION

Ephedrine is an indirectly acting sympathomimetic amine, a β agonist and weak central nervous system stimulant,

leading to norepinephrine release.¹ It is structurally similar to amphetamines, and has similar effects, including hypertension and tachycardia.¹ It is well-absorbed orally, and has peak plasma levels occurring within an hour of ingestion.² Dietary supplements that contain ephedrine and related ephedra alkaloids (also known as ma huang) are widely available, marketed for use in weight reduction and to help increase energy levels.³ Its thermogenic and lipolytic effects mean it is often combined with other drugs with similar effects, such as caffeine.⁴ Indeed, ephedrine and caffeine are thought to work synergistically.⁴ Caffeine increases the effect of ephedrine by interfering with a negative feedback system involving cyclic AMP (cAMP).⁴ Aspirin has a similar effect on this mechanism.⁴ Narnegin is a bioflavonoid derived from grapefruit, not thought to make a major contribution to the overall effects of the supplement.

There are several reports in the literature of significant adverse effects related to ephedrine containing supplements, including arrhythmias, myocardial infarction, stroke and seizures.³ The serious side effects are not necessarily dose-dependent, and serious adverse effects can occur in susceptible individuals with low doses.⁵ The toxic effects are worsened by dehydration, increased body temperature and physical exercise, clearly features likely to be present when ingested, as in this case.⁴ There have even been rare cases resulting in death from ephedrine toxicity, mainly from either myocardial infarction or stroke.² Thrombotic events such as myocardial infarction and ischaemic stroke are thought to be the result of arterial vasoconstriction and vasospasm.⁷ Haemorrhagic stroke is thought to be a result of ephedrine's hypertensive action, and association with cerebral vasculitis.⁷

In 2004, the evidence showing harm from its use led to a ban by the Food and Drug Administration in the USA.⁸ In sport, it has a threshold of 10 micrograms/millilitre in urine to be considered doping.⁹

There have been a few reported cases of healthy individuals suffering exercise induced rhabdomyolysis after taking supplements containing ephedrine.¹⁰ Typically they occurred in healthy individuals undertaking strenuous exercise who were dehydrated to begin with.¹¹ The man in this case was approximately 12 miles into his run, and had been having some flu like symptoms for the few days before the race, so may well have also been dehydrated.

The man in this case suffered two generalised tonic-clonic seizures. The first occurred when he became very hypoglycaemic, and may have been a result of this. However, the second occurred with normal blood glucose levels, and was possibly related to ephedrine toxicity, as has been previously reported.⁷

As many of these supplements are still easily available and either do not reveal all the ingredients, or contain the word 'natural', they are still widely used by often uninformed persons. There is also a well-known lack of knowledge among athletes using supplements,^{12–14} and so in the acute situation it may be difficult to ascertain what has been ingested. There is a growing trend in supplement use among athletes,¹⁵ and therefore presentation of patients

due to toxicity or related complications may become more common. Ephedrine containing supplements can have serious health consequences, occurring in often previously young and healthy individuals.

Learning points

- It is important to be aware of the possibility of the use of supplements in an acutely unwell person, especially who presents during or after a sporting event, and is otherwise healthy.
- A detailed drug history is vital, since patients often do not volunteer information on the use of supplements or herbal remedies.
- The consequences of toxicity also need to be identified, as it may contribute to later complications, such as rhabdomyolysis in this case.
- Knowledge among both athletes and healthcare professionals about dietary supplements needs to be improved.

Competing interests None.

Patient consent Obtained.

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