

# Profound hypokalaemia due to Nurofen Plus and Red Bull misuse

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## Clinical record

A 39-year-old man presented to our emergency department with a 3-day history of right leg weakness progressing to profound weakness of all limbs. There was no associated sensory disturbance or muscle tenderness, and there were no clinical features suggestive of either spinal or intracranial pathology.

His relevant past history included Tourette's syndrome, an obsessive-compulsive disorder, anxiety, depression, alcohol misuse and mild asthma, for which he was prescribed haloperidol, diazepam, alprazolam and salbutamol.

The patient disclosed that in the 3 days before being admitted, he had ingested 24 cans of Red Bull energy drink (6000 mL) and 2.5 bottles (1875 mL) of the homeopathic preparation, Nervatona Calm. He denied any other drug ingestion, vomiting or diarrhoea.

Examination revealed the patient to be afebrile, with stable vital signs. He had a severe symmetrical quadriplegia, more marked proximally, with preserved reflexes and normal findings on sensory examination, and without evidence of any muscle tenderness.

Initial investigations revealed profound hypokalaemia (1.8 mmol/L; reference range [RR], 3.5–5.0 mmol/L), hypophosphatemia (0.63 mmol/L; RR, 0.80–1.50 mmol/L) and a raised serum creatine kinase level (9394 IU/L; RR, 60–220 IU/L). Concentrations of the remainder of the serum electrolytes, including magnesium, serum urea and creatinine, were within normal limits; his urinary sodium concentration was 104 mmol/L and his urinary potassium concentration was 22 mmol/L. An electrocardiogram showed sinus rhythm with u waves.

Initial management in the emergency department included oral and intravenous potassium replacement. The patient was transferred to our intensive care unit, where he continued to receive intravenous potassium replace-

## ABSTRACT

We report an unusual and emerging cause of profound hypokalaemia associated with a severe myopathy, attributable to misuse of Nurofen Plus, a readily available over-the-counter medication containing ibuprofen and codeine, and excessive ingestion of the caffeine-containing energy drink, Red Bull. The mechanism of the hypokalaemia may be ascribed to ibuprofen-mediated type 2 renal tubular acidosis, and caffeine-mediated antagonism of adenosine receptors or intercompartmental shift of potassium into the intracellular space. Practitioners should be aware that patients with codeine addiction who misuse Nurofen Plus may present with severe hypokalaemia complicated by myopathy.

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ment at a maximum rate of 30 mmol/h. In total, he received 494 mmol of potassium replacement over the first 24 hours. His serum creatine kinase levels peaked at 46 298 IU/L at 48 hours, and subsequently fell (Table 1). Rhabdomyolysis was managed by establishing a high urine output at an alkaline pH.

After consultation with our Drug and Alcohol Service, it became apparent that our patient's female partner had recently been admitted to their service for management of withdrawal from the misuse of Nurofen Plus. On subsequent direct questioning, our patient volunteered that he had additionally ingested 72 Nurofen Plus tablets in the 3 days before his admission.

The patient was discharged to the ward, where his electrolyte levels remained satisfactory; he subsequently discharged himself from hospital against medical advice.

**Table 1. Sequential serum electrolyte and creatine kinase levels**

| Substance              | Time |       |        |        |        |        |       |
|------------------------|------|-------|--------|--------|--------|--------|-------|
|                        | 0 h  | 12 h  | 24 h   | 36 h   | 48 h   | Day 3  | Day 6 |
| Sodium (mmol/L)        | 141  | 149   | 148    | 144    | 139    | 143    | 140   |
| Potassium (mmol/L)     | 1.8  | 2.1   | 3.1    | 3.8    | 3.8    | 4.3    | 4.9   |
| Chloride (mmol/L)      | 106  | 113   | 117    | 113    | 109    | 112    | 109   |
| Creatine kinase (IU/L) | —    | 9 394 | 15 415 | 31 624 | 46 298 | 35 764 | 3 087 |

## Discussion

The cause of our patient's hypokalaemia was clouded by the unusually high doses of multiple substances ingested, including the retrospective history of misuse of Nurofen Plus. The 72 Nurofen Plus tablets he took, each containing 200 mg ibuprofen and 12.8 mg codeine phosphate, resulted in a total ingestion of 14 400 mg ibuprofen and 922 mg codeine.

We consider that our patient's hypokalaemia was most probably attributable to this significant ingestion, and we note previous case reports linking hypokalaemia with Nurofen Plus misuse.<sup>1-4</sup> In these previous reports, each of the four patients presented with profound hypokalaemia (ranging from 1.4 to 1.7 mmol/L) associated with variable degrees of muscle weakness after ingesting daily amounts of ibuprofen ranging from 4800 to 28 000 mg. One patient presented with quadriparesis, as did our patient, and two patients were noted to have high urinary potassium losses that were ascribed to type 2 renal tubular acidosis, a postulated mechanism for ibuprofen-mediated hypokalaemia. We note that our patient had an inappropriately raised urinary potassium concentration of 22 mmol/L at a time when his serum potassium concentration was only 2.1 mmol/L, despite ongoing potassium replacement therapy.

Another potential contributor to our patient's hypokalaemia and rhabdomyolysis may have been caffeine from his excessive consumption of Red Bull (80 mg caffeine/250 mL — a total of 1920 mg over 3 days). Toxic effects of caffeine include rhabdomyolysis and hypokalaemic myopathy, occurring with daily caffeine intakes ranging from 300 mg to 970 mg.<sup>5-7</sup> The mechanism of caffeine-mediated hypokalaemia may relate to antagonism of adenosine receptors, or alternatively, may have been caused by an intercompartmental shift of potassium into the intracellular space. While it is purported that Red Bull "gives you wings", we would caution that excessive consumption may potentially render people myopathic, due to caffeine-mediated hypokalaemia and rhabdomyolysis.

A further alternative cause for our patient's hypokalaemia may have been the excess ingestion of the homeopathic preparation Nervatona Calm, which is marketed as a remedy for stress. The dose recommended by the manufacturers is up to 60 mL daily, but our patient ingested 1875 mL over 3 days. Nervatona Calm contains a variety of extracts

from plants and plant roots, including anamirta cocculus, ignatia and nux vomica, which may cause rhabdomyolysis at toxic levels, but none of these agents have been associated with the development of hypokalaemia.

Because of the multiple and unusually high quantities of substances ingested by our patient, it is difficult to determine a single cause for his presentation. However, we note that prior clinical cases of Nurofen Plus misuse at similar levels without other confounding substances have also resulted in patients presenting with comparable significant hypokalaemia and weakness. The codeine content and ready availability of Nurofen Plus as an over-the-counter medication make it a potential drug for misuse.

Our case highlights the need for clinicians to recognise profound hypokalaemia and myopathy as a potential consequence of excessive Nurofen Plus ingestion. Moreover, misuse of Nurofen Plus should be considered in patients presenting with otherwise unexplained hypokalaemia.

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