



## Short Communication

# Syncope following intramuscular injection of hydroxocobalamin in a paraplegic patient: indication for oral administration of cyanocobalamin in spinal cord injury patients

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### Case report

This 81-year-old man joined the army in 1940 when he was 23. He was posted to the Far East in 1942 and was made a Prisoner of War in February that year in Singapore. After becoming a prisoner of war, he was mainly fed on rice. He developed complete loss of power and sensation in the right leg, weakness in the left leg, great weakness and some impairment of sensation in the right arm, and weakness in the left arm. At the same time he became almost blind and he noticed deafness in both ears. He had trouble in starting micturition. He was then put on a better diet and was given vitamin B tablets. After a month his sight was almost normal, but recovery of motor power was slower. Gradually he could get about with a stick. In August 1945, he was freed and returned to England. He has been getting vitamin B-12 injections on and off without side effects.

The results of routine tests performed on 29 October 1997 were as follows: serum vitamin B-12 level of 91 ng/l (reference range: 223–1132); folate level was 15.7 µg/l (reference range: 2.8–20.0); haemoglobin: 12.7 g/dl; MCV: 94.8 fl. He was prescribed intramuscular injections of 1 mg of Vitamin B-12 at intervals of 4–6 weeks. On 5 May 1998, he received an intramuscular injection of 1 mg of hydroxocobalamin without any adverse reaction. However when he received the next dose on 30 June 1998, he fainted about 10 min after the intramuscular injection. His blood pressure was 60/30 mmHg. He was given intravenous fluids. After 20 min the blood pressure increased to 110/60 mmHg. ECG showed sinus rhythm with non-specific T wave abnormality. Blood electrolytes and cardiac enzymes were within the normal range. Echo cardiography was normal. In August 1998, this

patient received the next dose of hydroxocobalamin (1 mg) by intramuscular injection; this was administered by a community nurse. He fainted soon after the injection and he was taken to the nearest emergency department. This time, apart from the syncope, he developed red patches and blisters over his arms, chest and legs. In view of the serious reaction to intramuscular injection of hydroxocobalamin, he was advised to take cyanocobalamin by mouth, 50 microgram tablets, two a day. Oral administration of radioactive vitamin B-12 without intrinsic factor resulted in 3.47% excretion in 24 h; B-12 with intrinsic factor led to urinary excretion of 1.49%. The vitamin B-12 levels are monitored every 3 months and the dose of cyanocobalamin will be increased, if necessary.

### Rationale for oral administration of vitamin B-12

The daily cobalamin turnover rate is about 2 µg. The mean absorption rate of oral cyanocobalamin by patients with pernicious anaemia is 1.2%. Therefore, an oral dose of 100–250 µg is sufficient for most patients. Due to individual variation in absorption, some patients have borderline serum levels when taking doses as high as 500 µg daily. In a study of 64 patients taking 500 µg daily, the lowest absorption rate was 1.8 µg/day, slightly less than the turnover rate. A dose of 1000 µg daily is therefore preferable. However, the recommended dose for the first month after a diagnosis of vitamin B-12 deficiency has been made is 2000 µg twice daily in order to rapidly replenish the body stores.<sup>1</sup> This patient had been receiving intramuscular injections of 1 mg of vitamin B-12; therefore, he requires only maintenance dose of vitamin B-12. The use of doses that are excessive for most patients is acceptable because cobalamin is inexpensive, and is widely considered to have a low order toxicity. The cobalt and cyanide contributions from 1000 µg/day

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of vitamin B-12 as cyanocobalamin are toxicologically insignificant.<sup>2</sup>

### Adverse reactions to vitamin B-12

The Committee on Safety of Medicines (personal communication) has received reports of three cases of syncope and one case of hypotension following hydroxocobalamin injection. Woodliff<sup>3</sup> reported allergic reaction to cyanocobalamin injection in an old lady who developed a generalised erythematous skin rash. This patient was subsequently treated by oral administration of 125 µg of vitamin B-12 daily; this caused no reaction and her serum vitamin B-12 level remained within the normal range. Ugwu and Gibbins<sup>4</sup> described hypotension and peripheral vascular collapse after 500 µg of hydroxocobalamin injection in an 89-year-old female with no significant past medical illness or history of allergy. Prior to this reaction, the patient tolerated vitamin B-12 injections for 5 years without incident. Subsequently, this patient was placed on oral cyanocobalamin 50 µg daily and showed no adverse reactions whatsoever. The patient reported by us had also received intramuscular injections of vitamin B-12 in the past without incident. Thus it appears that an allergic reaction to vitamin B-12 injection can suddenly occur in patients who had received intramuscular injection of vitamin B-12 without any adverse reaction for many years. Woodliff<sup>3</sup> stated that a death has been noted as a result of reaction to vitamin B-12. The fact that reactions, including anaphylactic shock, can occur to vitamin B-12 reinforces the practice that adrenaline and a parenteral antihistamine preparation should always be available when injections of vitamin B-12 are being given.

### Vitamin B-12 deficiency in paraplegic and tetraplegic subjects

Vitamin B-12 deficiency may not be uncommon among paraplegic and tetraplegic subjects, especially among the elderly. During 1997–98, four patients were diagnosed to have vitamin B-12 deficiency in the Regional Spinal Injuries Centre, Southport (Table 1). In patients referred to a geriatric medical unit in Glasgow, 13% had a low serum vitamin B-12 level; mean haemoglobin levels were not significantly reduced in those with a low vitamin B-12.<sup>5</sup> Some spinal cord injury patients may have continent urinary reservoirs; a few may undergo lower urinary tract reconstruction with ileum. These patients are at risk for developing vitamin B-12 deficiency. A few paraplegic/tetraplegic patients (eg case number 3 in the table) may develop vitamin B-12 deficiency of nutritional origin if the dietary intake comprises mainly chips, ice-cream, fruit and Coca-cola.

### Screening for vitamin B-12 deficiency and oral administration of vitamin B-12 in spinal cord injury persons

We suggest that vitamin B-12 levels should be checked during annual review in (1) elderly spinal cord injury patients, (2) those who have undergone urinary intestinal diversion or lower urinary tract reconstruction with ileum, (3) vegans or, (4) those who have dietary fads. Cyanocobalamin tablets are not approved for prescription in the National Health Service except to treat or prevent vitamin B-12 deficiency in a patient who is a vegan or who has a proven vitamin B-12 deficiency of dietary origin.<sup>6</sup> Oral administration of

**Table 1** Clinical and haematological details of paraplegic and tetraplegic patients who had low serum vitamin B-12 levels (normal range: 223–1, 132 ng/l)

Case no.	Sex	Year of birth	Diagnosis	Date when paralysed	Date of sampling	Vitamin B-12 level	Presenting clinical symptom	Full blood count results
1	M	1924	Traumatic tetraplegia C-4 complete	23/07/1997	31/12/1997	94	–	Haemoglobin: 15.3 MCV: 98.1
2	M	1923	Traumatic tetraplegia C-5	18/08/1990	21/09/1998	87	–	Haemoglobin: 12.1 MCV: 87.9
3	F	1973	Spina Bifida and paraplegia	Since birth	30/12/1997	94	–	Haemoglobin: 6.5 MCV: 112.8 Blood film: oval macrocytes, hyper-segmented neutrophils, tear drop poikilocytes – compatible with vitamin B-12 deficiency
4	F	1943	Tramatic tetraplegia with phrenic pacer	30/05/1997	11/12/1997	173	Confusion	Haemoglobin: 11.8 MCV: 105 Blood film: macrocytes+; anisocytosis; target cells+

vitamin B-12 may be indicated in spinal cord injury patients who develop allergic reaction to intramuscular injection (as in the case depicted above), and in the elderly spinal cord injury patients who do not suffer from pernicious anaemia or intestinal malabsorption. Low vitamin B-12 serum levels in older people have been restored to normal range by oral administration.<sup>7</sup>

### Acknowledgements

Our gratitude to: Dr PC Waller, Specialist in Pharmacovigilance, Post-Licensing Division, Medicines Control Agency, London for permitting us to use MCA data in this manuscript; Dr B Woodcock, Consultant Haematologist, District General Hospital, Southport for reviewing the manuscript and providing critical comments; Mr Dinesh K Mehta, Executive Editor, British National Formulary for valuable advice.

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