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CLINICAL RESEARCH STUDY

Food-cobalamin malabsorption in elderly patients: Clinical manifestations and treatment

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Elderly patients;
Atrophic gastritis;
Drugs;
Oral cobalamin treatment

ABSTRACT

PURPOSE: Approximately 15% of people aged more than 60 years old have a cobalamin (vitamin B12) deficiency, mainly in relation with food-cobalamin malabsorption (FCM). To date, no study has documented this disorder in the elderly. There is also little information on clinical consequences.

SUBJECTS AND METHODS: We studied 92 elderly patients with well-established FCM who were extracted from an observational cohort study (1995-2004) of 172 consecutive elderly patients with documented cobalamin deficiency.

RESULTS: The median patient age was 76 ± 8 years; 60 patients were women. The most common clinical manifestations were neurologic or psychologic: mild sensory polyneuropathy (44.6%), confusion or impaired mental functioning (22.8%), and physical asthenia (20.7%). Hematologic abnormalities were reported in at least one third of the patients: anemia (21%), leukopenia (10.9%), thrombopenia (8.7%), and pancytopenia (6.5%). All patients had low serum vitamin B12 levels (<200 pg/mL), with a mean value (± standard deviation) of 131 ± 38 pg/mL and total serum homocysteine level of 22.1 ± 9.3 μmol/L. The mean hemoglobin level was 10.9 ± 2.5 g/dL and the mean erythrocyte cell volume 95.7 ± 12.7 fL. Correction of the serum vitamin B12 levels and hematologic abnormalities was achieved equally well in patients treated with either intramuscular or oral crystalline cyanocobalamin.

CONCLUSIONS: This study suggests that in elderly patients, FCM may be associated with significant neurologic, psychologic, and hematologic abnormalities, which seem to respond equally well to either oral or parenteral vitamin B12 therapy.

A recent population survey revealed that 15% of people aged more than 60 years had undiagnosed cobalamin (vitamin B12) deficiency.[1] Although only a minority of such persons display clinically obvious symptoms or signs, metabolic data clearly show a cellular deficiency of cobalamin in most cases. The evidence suggests that this is not a normal physiologic expression of the aging process.[2] Classic disorders such as pernicious anemia are the cause of this deficiency in only a limited proportion of the elderly.[3] A more frequent problem is food-cobalamin malabsorption (FCM),[2,4] a disorder characterized by the inability to release vitamin B12 from food or its binding protein.[5,6] Thus, patients have low serum vitamin B12 levels, normal Schilling test results, and commonly an atrophic gastritis. To date, only case reports or small studies have documented this syndrome in elderly patients.[3,7] This article presents data of

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a cohort study of 92 elderly patients with confirmed cobalamin deficiency related to FCM.

Patients and methods

Selection of patients

Between January 1995 and January 2004, all patients aged more than 65 years who were identified as having a confirmed cobalamin deficiency were enrolled in an observational cohort study (preliminary data[7] published in 2002). All of these elderly patients were initially screened for cobalamin deficiency mainly because of neuropsychiatric manifestations or hematologic abnormalities. Cobalamin deficiency was defined according to the criteria of Snow[8] and Klee[9]: a serum cobalamin level less than 200 pg/mL confirmed in 2 serum samples or in association with a total homocysteine level greater than 13 μmol/L. The latter criterion was only used if there was normal renal function (serum creatinine level $<$120 μmol/L).[10] The patients were recruited from the Departments of Internal Medicine and Geriatrics of the Hôpitaux Universitaires de Strasbourg, France. Of these elderly patients, those with established cobalamin deficiency related to FCM were identified. FCM was defined according to the criteria of Carmel[6,11]: low serum vitamin B12 level; normal Schilling test result using free 58Co-cyanocobalamin and intrinsic factor-bound 57Co-cyanocobalamin; lack of serum antibodies to intrinsic factor[12]; and daily intake of vitamin B12 of at least 5 μg[13] (Table 1).

Table 1 Syndrome of food-cobalamin malabsorption

Criteria for FCM:
- Low serum vitamin B12 levels
- Normal results of Schilling test using free cyanocobalamin labeled with cobalt-58 or abnormal results of derived Schilling tests*
- No anti-intrinsic factor antibodies
- No dietary cobalamin deficiencies

Associated agents and/or clinical conditions:
- Gastric disease: atrophic gastritis, type A atrophic gastritis, gastric disease associated with *Helicobacter pylori* infection, partial gastrectomy, gastric bypass (obesity), vagotomy
- Pancreatic insufficiency: alcohol abuse, cystic fibrosis
- Gastric or intestinal bacterial overgrowth: achlorhydria, tropical sprue, Ogylvie syndrome, HIV
- Drugs: acid-suppressive drugs (cimetidin, ranitidin, omeprazol) or biguanides (metformin)
- Alcohol abuse
- Sjögren syndrome, systemic sclerosis
- Haptocorrine deficiency
- Ageing or idiopathic

FCM = food-cobalamin malabsorption.

Adapted from Andrès E, Perrin AE, Demangeat C, et al. The syndrome of food-cobalamin malabsorption revisited in a Department of Internal Medicine. A monocentric cohort study of 80 patients. *Eur J Intern Med*. 2003;14:221–226, with permission.

*Derived Schilling tests used food-bound cobalamin (eg, egg yolk).

Analyzed data

All data were obtained retrospectively from medical records, including history of drugs or alcohol intake, clinical status, relevant biochemical data (eg, serum vitamin B12 and total homocysteine levels), blood cell count, and bone marrow examination (when available). Other data included Schilling test results, anti-intrinsic factor antibody levels, estimated daily intake of vitamin B12, evidence of *Helicobacter pylori* infection (using a rapid urease testing and histologic examination of gastric biopsy specimens), and findings on upper endoscopy (if performed). Treatment data, including method of administration (oral or parenteral) and doses of vitamin B12, were recorded when available, as were the immediate and long-term outcomes.

Laboratory methods

Serum vitamin B12 levels (normal range: 200-1100 pg/mL) were determined by radioimmunoassays or enzyme immunoassay using commercial kits: radioimmunoassay (Bayer Corp., New York, NY) or enzyme immunoassay (Abbott, Rungis, France). Total serum homocysteine (normal range: 6-12 μmol/L) was measured using capillary gas chromatography-mass spectrometry. Serum anti-intrinsic factor antibodies were measured using commercial kits: enzyme-linked immunosorbent assay (Bayer Corp.). An automated Coulter counter (Technikon H1; Bayer Corp.) was used to measure hematologic parameters. For the first 68 patients, the Schilling test was realized with commercial kits: Dicopac test (Amersham Healthcare, Buckinghamshire, UK). The Schilling test result was considered normal if the ratio factor of intrinsic bound vitamin (57Co) and free vitamin (58Co) was between 0.7 and 1.2. For the remaining patients, Schilling tests were performed as follows: Patients were administered 1000 μg of cyanocobalamin intramuscularly on day 1 and 1000 μg of free 58Co-vitamin orally on day 2. The patient's urine was then collected for 24 hours (from day 2 to day 3), and the percentage of labeled cyanocobalamin was determined to rule out malabsorption and pernicious anemia.

Therapeutic regimens

Intramuscular cyanocobalamin (Vitamine B12, Mille Delagrange Synthelabo, Meudon-la-Forêt, France, or Vitamine B12, Aguettan, Lyon, France) was administered at a monthly dose between 500 and 1000 μg. Oral crystalline cyanocobalamin (Vitamine B12, Mille Delagrange Synthelabo, or Vitamine B12, Aguettan) was administered at a daily dose between 125 and 1000 μg.