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Nutritional Anemia in Elderly Patients of Developed Countries

Emmanuel Andrès

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Abstract

In this chapter, we report and discuss the current literature of nutrient-deficiency anemia, also called nutritional anemia, in elderly patients in developed countries. For this purpose, a review of medical literatures was conducted searching PubMed, textbooks of hematology, internal medicine and geriatrics, and information collected from international meetings were also included. The term nutrient deficiency or nutritional anemia covers any anemia, defined by a hemoglobin level <13 g/dL (<130 g/L) in men and <12 g/dL (<120 g/L) in women, resulting from a deficiency of materials essential for erythropoiesis. Patients with nutritional anemia often have mild to moderate anemia, with hemoglobin levels between 8 and 10 g/dL (80 and 100 g/L). In practice, nutritional anemia represents one-third of all anemia in elderly patients. About two-third of nutritional anemia is associated with iron deficiency and most of those cases are the result of chronic blood loss from gastrointestinal lesions. The remaining cases of nutritional anemia are usually associated with vitamin B12 (cobalamin), most frequently related to food-cobalamin malabsorption (especially in case of atrophic gastritis), and Biermer’s disease (pernicious anemia); and/or vitamin B9 (folate) deficiency, most frequently related to inadequate dietary intake or malnutrition, several drugs (as methotrexate, cotrimoxazole) and chronic alcohol intake. In clinical practice, recognition of these disorders and deficiencies is essential for optimal treatment (nutrient-deficiency replacement).

Keywords: nutritional anemia, nutrient-deficiency anemia, iron deficiency, vitamin B12 deficiency, cobalamin deficiency, vitamin B9 deficiency, folate deficiency, food

1. Introduction

Anemia is a common condition, especially in elderly patients (≥75 years) and its prevalence increases with age [1]. Anemia affects quality of life in all elderly patients. It also affects cognitive and physical function, especially in frailty patients, and be a factor of aggravation or poor
prognosis of chronic diseases, e.g., chronic heart failure (CHF), chronic obstructive pulmonary disease (COPD), chronic renal failure, cerebrovascular disorders [2, 3]. Anemia is even associated with a risk of death. Thus, it should not be accepted as an unavoidable condition or a consequence of aging.

In the elderly, many underlying conditions can lead to anemia such as chronic diseases, renal failure, myelodysplastic syndromes, cancer, and unexplained anemia. However, the most common nutrient deficiencies are iron, vitamin B9 (folic acid), and vitamin B12 (cobalamin) deficiency [4]. In clinical practice, recognition of these disorders and deficiencies is essential for optimal treatment.

In this chapter, we report and discuss the current literatures of nutrient-deficiency anemia, also called nutritional anemia, in elderly patients in developed countries.

2. Bibliographic search strategy

A review of the medical literatures was conducted to identify original studies and review articles concerning nutrient-deficiency anemia in elderly patients. In March 2017, PubMed was searched for English- and French-language articles. The terms used for online bibliographic search included “nutrient-deficiency anemia,” “nutritional anemia,” “iron deficiency,” “vitamin B9 deficiency,” “folate deficiency,” “vitamin B12 deficiency” or “cobalamin deficiency,” and “elderly patients.” A total of more than 500 abstracts related to clinical trial and reviews were identified between the years 2007 and 2017. All of the abstracts were reviewed by at least two senior researchers. Only 245 publications were eventually retained and 39 publications were used for this review. These publications have been selected because of the quality or the originality of the text, the excellence of the adopted methodology, and the reputation of the authors.

Textbooks of hematology, internal medicine and geriatrics, and information collected from international meetings were also included.

3. Definition of nutritional anemia

The World Health Organization (WHO) defines anemia in the adult as hemoglobin (Hb) concentration < 12 g/dL (<120 g/L) for nonpregnant women and <13 g/dL (<130 g/L) for men [2]. In elderly, an Hb concentration < 12 g/dL (<120 g/L) is commonly considered as an “established” anemia (under strict sense of the academic definition), regardless of the sex of the patient [5].

Although low hemoglobin levels (approximately 1 g/dL lower than the WHO standard) are often seen with advancing age, anemia (called “unexplained” anemia) should not be assumed to be a normal consequence of aging. Several age-related physiological changes such as renal insufficiency, stem cell aging, androgen insufficiency, and chronic inflammation may contribute either to a decline in red blood cell production or shortened red blood cell survival.
Age may be associated with compromised hematopoietic reserve and consequently with an increased susceptibility to anemia in the presence of hematopoietic stress induced by an underlying disorder [6].

In clinical practice, an Hb level <10 g/dL is often considered to be a cut off level where investigation in the elderly (“anemia to explore”), and treatment should be performed [7]. Indeed, at this Hb level, several recent studies have shown a benefit from investigating the anemia and for treating, in regard to the frequency of discovery of a curable etiology [7].

Nutrient-deficiency or nutritional anemia refers to types of anemia that can be directly attributed to “nutritional disorders” [4, 8]. Thus, the term nutrient deficiency or nutritional anemia covers any anemia resulting from a deficiency of nutrients essential for red blood cell formation, for example: iron; vitamins, especially vitamin B9 (folate), but also vitamin B12 (cobalamin) and vitamin C (in scurvy), and more rarely, vitamin A, vitamin E, and vitamin B2 (riboflavin), vitamin B3 (in pellagra), vitamin B6 (pyridoxine); selenium, zinc, and cooper; and protein [8].

4. Prevalence of nutritional anemia

The prevalence of anemia increases with advancing age, especially after age 60–65 years, and rises sharply after the age of 80 years [2, 6]. Currently, anemia in this population represents a public health problem in developed countries.

In the United States (US), results from the third National Health and Nutrition Examination Survey (NHANES III) indicate that the prevalence of anemia among elderly individuals, living in towns, aged 75 or more and 85 or more, were 15.7% in men and 10.3% in women and 26.1% for men and 20.1% in women, respectively [1]. Survey findings indicate further that most anemia among the middle age and elderly is mild; only 2.8% of women and 1.6% of men had an Hb <11 g/dL [9]. Results from the NHANES III also indicate that nutrient-deficiency anemia represents at least one-third of all causes of anemia [1].

In the US, results from the Framingham cohort indicate a lower prevalence of anemia among 1016 subjects within 67–96 years of age. In this group, the prevalence of anemia in men and women was 6.1 and 10.5%, respectively [10]. In this study, in addition to anemia of inflammation and of renal failure, nutritional anemia was also a major cause of anemia.

In a French nationwide study of 1351 patients hospitalized in several departments of Internal Medicine, anemia was present in 874 (65%) patients according to the WHO definition, and 573 (42%) patients had an Hb level of <11 g/dL (<11 g/L) [11].

5. Etiology of anemia with a focus on nutritional anemia

Because elderly patients often have several associated co-morbid conditions and are commonly taking a variety of medications, some of which may contribute to anemia, the precise etiology of anemia is frequently difficult to determine, even after extensive investigations, including bone marrow biopsy [3, 13]. Thus, according to the literatures and in our own experience, the
etiology of anemia can be identified in only approximately 80% of the cases, in spite of the use of new tools such as video capsule [7, 14]. Moreover, a significant proportion of elderly anemic patients, around 30–50%, are presumed to have multiple causes for their anemia [14, 15]. In cases where the causes of anemia have not been established, an inadequate diagnostic work-up for the patient could be suspected.

In the elderly, causes of anemia are divided into three main broad groups: (1) “nutrient-deficiency or nutritional anemia,” mainly in relation with iron deficiency anemia; (2) “anemia of chronic disease,” including anemia related to renal failure, chronic inflammation, chronic heart failure; and (3) “unexplained anemia” [2, 3, 9]. In the aforementioned NHANES III study, 34% of all anemia in adults and elderly patients were caused by iron, vitamin B9 (folate), and vitamin B12 (cobalamin) deficiency, alone or in combination (nutrient-deficiency anemia) [1]. In this study, 12% of all anemia were related, perhaps at least associated, with renal insufficiency, 20% with chronic diseases, and in 34% of the cases, the cause of anemia remained unexplained.

About 60% of nutritional anemia is associated with iron deficiency and most of those cases are the result of chronic blood loss from gastrointestinal lesions in developed countries [1]. The remaining cases of nutrient-deficiency anemia are usually associated with vitamin B12 and/or vitamin B9 deficiency and are easily treated. In Table 1, we report our personal experience (retrospective study) of the etiology of anemia in 300 hospitalized patients of ≥65 years old [4, 7].

Rare unknown causes of nutrient-deficiency anemia include several other vitamin deficiencies (e.g., vitamins A, B2, B3, C, and E), selenium, zinc, or cooper [8]. These later etiologies are nevertheless not well-studied in the literature, and to date, few not well-documented data are available, except for the theoretical and pathological aspects of anemia.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic inflammation (chronic disease)</td>
<td>23.0</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>18</td>
</tr>
<tr>
<td>Renal failure</td>
<td>9</td>
</tr>
<tr>
<td>Liver disease and endocrine disease (chronic disease)</td>
<td>7</td>
</tr>
<tr>
<td>Posthemorrhagic</td>
<td>7</td>
</tr>
<tr>
<td>Folate deficiency</td>
<td>6</td>
</tr>
<tr>
<td>Myelodysplasia</td>
<td>5</td>
</tr>
<tr>
<td>Vitamin B12 deficiency</td>
<td>4</td>
</tr>
<tr>
<td>Unexplained causes</td>
<td>21</td>
</tr>
</tbody>
</table>

Table 1. Etiology of anemia in patients older than 65 years (n = 300), hospitalized in an internal medicine department (tertiary reference center) [7].
6. Iron deficiency anemia in the elderly

Iron deficiency anemia, the most common cause of anemia in the elderly [1], results usually from chronic gastrointestinal (GI) blood loss mainly caused by esophagitis, gastritis, ulcer, related or not related to nonsteroidal anti-inflammatory drug intake, and/or chronic Helicobacter pylori infections, varices (portal hypertension), premalignant polyps, colorectal cancer, or angiodysplasia [15, 16].

It is important to keep in mind that GI blood loss is often occult and is not ruled out by negative fecal blood tests. In elderly, GI tract abnormalities can be identified with appropriate investigations (mainly invasive and require general anesthesia) in the majority of patients with iron deficiency anemia [14]. In 40–60% of patients, the source is in the upper GI tract and the identified cause of GI blood loss is benign [18, 19]. In 15–30% of patients, the source of GI blood loss is in the colon, here also with mainly benign lesions. Table 2 presents our experience of the evaluation of the GI tract in 90 patients with chronic blood loss during their follow-up in an internal medicine department (in a referral center) [7].

The source of bleeding is not found in the remaining 10–40% of patients with GI blood loss. Fortunately, these patients do well with iron replacement and repeated investigation may be only proposed in “to good health” elderly patients [15]. In these patients, repeated GI investigation with upper and/or lower endoscopy and video capsule may be of interest, with the detection of the etiology of bleeding in an additional 20% of cases [19, 20]. It is important because one-third of the iron deficiency anemia is related to GI malignancies. In our experience, repeated investigation is not recommended in frailty elderly patients [21].

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagitis and Mallory Weiss syndrome</td>
<td>4.4</td>
</tr>
<tr>
<td>Gastritis, atrophic gastritis and ulcer related or not related to NSAID use and/or Helicobacter pylori infection</td>
<td>30</td>
</tr>
<tr>
<td>Varices related to portal hypertension</td>
<td>9</td>
</tr>
<tr>
<td>Angiodysplasia</td>
<td>2.25</td>
</tr>
<tr>
<td>Colon diverticula</td>
<td>4.5</td>
</tr>
<tr>
<td>Colorectal benign and pre-malignant polyps</td>
<td>5.5</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>5.5</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>2.25</td>
</tr>
<tr>
<td>Unexplained causes</td>
<td>36.6</td>
</tr>
</tbody>
</table>

NSAID: nonsteroidal anti-inflammatory drug.

Table 2. Results of the evaluation of the gastrointestinal tract in elderly patients (≥65 years) with chronic blood loss (n = 90), hospitalized in an internal medicine department [14].
H. pylori infection, chronic gastritis (especially atrophic gastritis), and coeliac disease are associated with “unexplained GI iron deficiency anemia” [22]. More rarely, large amount of tea (at least 2 L/day), vegetarian and theoretically long-term anti-acid medication intake are also associated with this condition [15]. In practice, any elderly subject whose dietary intake is poor and has recent unexplained weight loss is a candidate for increased medical surveillance [23].

Chronic blood loss from the genitourinary tract and exceptionally from chronic hemoptysis may result in iron deficiency [15]. In this situation, bleeding disorders and particularly anticoagulant and antiplatelet medications may promote the development of iron deficiency in the elderly (around 20% in our experience) [7, 14].

7. Vitamin B9 and vitamin B12 deficiency anemia in the elderly

Both vitamin B9 and B12 deficiencies are common among elderly, each occurring in at least 5% of the patients [15]. The Framingham study demonstrated an incidence of 12% among elderly people living in the community [24].

Vitamin B9 deficiency usually develops as a result of inadequate dietary intake and malnutrition, quiet frequent in elderly patients of malabsorption, as in coeliac disease [1, 15]. In fact, a regular diet contains 500–700 μg of vitamin B9 and the body contains very little vitamin B9 with stocks expected to last 4–6 months. The affected patients usually have a history of weight loss, poor weight gain, and weakness. This is particularly the case in Alzheimer’s patient or in patients with advanced dementia. In addition, several drugs (methotrexate, cotrimoxazole, sulphasalazine, anticonvulsants) and alcohol—even in elderly—may cause deficiency of folic acid [7].

In elderly patients, the etiologies of vitamin B12 deficiency are represented primarily by food-cobalamin malabsorption (FCM) and Biermer’s disease, also called pernicious anemia. The FCM is not a real malabsorption in view of physiopathology, but a maldigestion of vitamin B12 (linked to food). More rarely, the etiologies of vitamin B12 deficiency include intake deficiency and true malabsorption, related for example, to digestive tract surgery [25]. In a study by our group (n = 200), FCM accounted for about 60–70% of the etiologies of vitamin B12 deficiency and about 15–25% in Biermer’s disease [26, 27]. Figure 1 presents the principal causes of vitamin B12 deficiency in 172 elderly patients (median age: 70 years) hospitalized in the University Hospital of Strasbourg, France [26].

FCM is characterized by the inability to release cobalamin from food and/or intestinal transport proteins, particularly in case of hypochlorhydria, where the absorption of “unbound” cobalamin is normal (“mal digestion” of the food-cobalamin) [28]. As we have recently indicated, this syndrome is defined by cobalamin deficiency despite sufficient cobalamin intake from food and a normal Schilling test, where the later rules out malabsorption or pernicious anemia [29]. FCM is caused primarily by atrophic gastritis [28]. Other factors that commonly contribute to FCM in elderly people include chronic carriage and infection of H. pylori; intestinal microbial proliferation; long-term ingestion of antacids (e.g., proton-pump inhibitors), and biguanides (metformin); chronic alcoholism; surgery or gastric reconstruction (e.g., bypass surgery for obesity); partial and pancreatic exocrine failure [29]. It should be emphasized that
Carmel first believed that FCM was associated with moderate cobalamin deficiency, leading to only “subtle” clinical symptoms (“subtle cobalamin deficiency”) [30]. However in our experience, the clinical manifestations of FCM are not very different from those of cobalamin deficiencies associated with other causes, e.g., Biermer’s disease [29].

Biermer’s disease is caused by impaired absorption of vitamin B12 due to the neutralization of intrinsic factor action in the setting of immune atrophic gastritis (loss of intrinsic factor in genetic form) [4, 25]. In practice, the diagnosis of Biermer’s disease is based on the presence of: (i) intrinsic factor antibodies in serum (specificity: >98%, sensibility: around 50%) and/or (ii) autoimmune atrophic gastritis (the presence of *H. pylori* infection in gastric biopsies is an exclusion factor) [4, 25]. It is to note that Biermer’s disease is associated with other immunological diseases, even in the elderly, such as Sjögren’s syndrome, Hashimoto’s disease, type 1 diabetes mellitus, or coeliac disease.

8. Clinical presentation of nutritional anemia

In elderly patients, the onset of anemic symptoms (fatigue, asthenia) and signs (pallor, palpitations) is usually insidious because majority of these patients adjust their physical activities, stay at home, and take several drugs which mask the anemic symptomatology. Thus, these symptoms may be overlooked and undiagnosed. [15]. In elderly, anemia may be revealed by the exacerbation of chronic-associated conditions or disorders, as dyspnea or edema of the legs related to worsening of cardiac failure. Anemia has also been reported to worsen angina, cognitive dysfunction related to cerebrovascular insufficiency [6].

In elderly patients, anemia has been associated with an increased risk for mortality, a longer hospitalization for elective procedures and a decreased quality of life [6, 31].

Iron, vitamin B9, and vitamin B12 deficiencies may be associated with specific symptoms and clinical manifestations. Table 3 presents features related to vitamin B12 deficiency.
in elderly patients [25]. The features of vitamin B9 deficiency are nearly indistinguishable from those of vitamin B12 deficiency, although the symptomatology is generally less severe. Iron deficiency is responsible for changes in hair (hair loss), nails (koilonychias), glossitis, dermatitis herpetiformis, photodermatitis, restless legs syndrome, and/or Plummer’s syndrome [32].

9. Biological abnormalities related to nutritional anemia

Patients with nutritional anemia often have mild to moderate anemia, with Hb levels between 8 and 10 g/dL. This anemia is generally hyporegenerative, with a low reticulocyte count (<50 × 10^9/L). This represents the consequence of the reduced activity of the hematopoietic system to replace the peripheral blood loss or deficiency [12, 15].

In elderly, the anemia is frequently “normocytic,” with a mean erythrocyte cell volume (MECV) between 80 and 100 fL. This normocytic nature of the anemia is related to the multifactorial etiologies of anemia. In exclusive iron deficiency, the erythrocytes are usually “microcytic,” with a MECV <80 fL (main differential diagnoses: chronic inflammation, thalassemia). In exclusive vitamin B9 and/or vitamin B12 deficiency, the erythrocytes are usually “macrocytic,” with a MECV >120 fL (main differential diagnosis: alcohol, hypothyroidism, and myelodysplastic syndromes). Other hematological abnormalities and manifestations may also be associated with cobalamin deficiency as listed in Table 4 [33].

Iron deficiency is documented by a low serum iron level, an increased total iron-binding capacity, and a low serum ferritin level (<15 ng/mL) [17]. In cases associated with chronic inflammation, the transferrin receptor-ferritin index appears to be the most appropriate parameter to discriminate between the two disorders [17].
Vitamin B12 deficiency is usually documented by a low serum vitamin B12 level (<200 pg/mL). An increase of the serum methylmalonic acid or homocysteine levels should be established to exclude a false negative result for vitamin B12 [30]. In vitamin B9 deficiency, the red cell vitamin B9 concentration is the recommended investigation [30].

### Table 4. Hematological manifestations in patients with documented cobalamin deficiency (n = 201), hospitalized in an internal medicine department (tertiary reference center) [33].

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin level (g/dL)</td>
<td>10.3 ± 0.4 (4.9–15.1)</td>
</tr>
<tr>
<td>Mean erythrocyte cell volume (fL)</td>
<td>98.9 ± 25.6 (76–142)</td>
</tr>
<tr>
<td>Reticulocyte count (%)</td>
<td>15.2 (1–32)</td>
</tr>
<tr>
<td>White cell count (/mm³)</td>
<td>6200 ± 4100 (500–20,000)</td>
</tr>
<tr>
<td>Platelet count (10⁹/mm³)</td>
<td>146 ± 42 (27–580)</td>
</tr>
<tr>
<td>Anemia with Hb level &lt; 12 g/dL</td>
<td>37%</td>
</tr>
<tr>
<td>Anemia with Hb level &lt; 6 g/dL</td>
<td>2.5%</td>
</tr>
<tr>
<td>Anemia and macrocytosis (MECV &gt;100 fL)</td>
<td>33.8%</td>
</tr>
<tr>
<td>Isolated macrocytosis (MECV &gt;100 fL)</td>
<td>17%</td>
</tr>
<tr>
<td>Microcytosis (MECV &lt;80 fL)</td>
<td>5%</td>
</tr>
<tr>
<td>White cell count &lt;4000/mm³</td>
<td>14%</td>
</tr>
<tr>
<td>Neutrophil count &lt;1000/mm³</td>
<td>3%</td>
</tr>
<tr>
<td>Thrombopenia (&lt;150 × 10⁹/mm³)</td>
<td>10%</td>
</tr>
<tr>
<td>Neutrophil hypersegmentation</td>
<td>32%</td>
</tr>
<tr>
<td>Megaloblastosis</td>
<td>60%</td>
</tr>
<tr>
<td>Life threatening manifestations</td>
<td>9%</td>
</tr>
</tbody>
</table>

MECV: mean erythrocyte cell volume.

Vitamin B12 deficiency is usually documented by a low serum vitamin B12 level (<200 pg/mL). An increase of the serum methylmalonic acid or homocysteine levels should be established to exclude a false negative result for vitamin B12 [30]. In vitamin B9 deficiency, the red cell vitamin B9 concentration is the recommended investigation [30].

### 10. Treatment of nutritional anemia

In iron deficiency anemia, iron supplementation should be initiated in association with the treatment of the underlying cause of bleeding. Treatment of nutritional anemia requires particular attention to establish the correct cause in all patients, particularly in elderly patients in a very good general condition of the body or mind [15]. Standard therapy for iron deficiency is an oral administration of 200–300 mg of ferrous sulfate (60 mg of elemental iron) [34, 35]. Oral iron supplementation is usually the first choice for the treatment of iron deficiency anemia because of its effectiveness and low cost. Vitamin C enhances iron absorption. Intravenous iron replacement may be reserved for patients with iron deficiency that fails to respond to oral replacement.
or in patients with documented malabsorption, inflammatory bowel diseases, malignancies, renal failure, and also perhaps in anemic patients with chronic heart failure. Parenteral iron supplementation may also be used when there is an intolerance or noncompliance with oral preparations. Intravenous iron sucrose is reasonably well tolerated, even when administered in boluses [35].

In elderly patients, vitamin B12 deficiency anemia may be treated by vitamin B12 supplementation, parenterally (commonly intramuscular) or orally [36, 37]. Our team (CAREnce en vitamine B12 [Care B12]) in the University Hospital of Strasbourg (France) has developed an effective oral treatment for cobalamin deficiency. The main results of our protocol of oral cobalamin therapy studies are summarized in Table 5 [36]. A systematic review conducted under the auspices of the Cochrane Metabolic and Endocrine Disorders Review Group also supports the efficacy of oral cobalamin therapy, with: (1) a daily dose of 2000 and 1000 μg for 1 month of crystalline cyanocobalamin.

<table>
<thead>
<tr>
<th>Study characteristics (number of patients)</th>
<th>Therapeutic modalities</th>
<th>Results</th>
</tr>
</thead>
</table>
| Open prospective study of well-documented vitamin B12 deficiency related to food-cobalamin malabsorption (n = 10) | Oral crystalline cyanocobalamin: 650 μg/day, during the condition and continue at least 3 months | • Normalization of serum vitamin B12 levels in 80% of the patients  
• Significant increase of Hb levels (mean of 1.9 g/dL) and decrease of MECV (mean of 7.8 fl) |
| Open prospective study of low vitamin B12 levels not related to pernicious anemia (n = 20) | Oral crystalline cyanocobalamin: 1000 μg/day during the condition and continue at least 1 week | • Normalization of serum vitamin B12 levels in 85% of the patients |
| Open prospective study of well-documented vitamin B12 deficiency related to food-cobalamin malabsorption (n = 30) | Oral crystalline cyanocobalamin: between 1000 and 250 μg/day, during the condition and continue at least 1 month | • Normalization of serum vitamin B12 levels in 87% of the patients  
• Significant increase of Hb levels (mean of 0.6 g/dL) and decrease of MECV (mean of 3 fl); normalization of Hb levels and MECV in 54 and 100% of the patients, respectively  
• Dose effect–effectiveness dose of vitamin B12 ≥500 μg/day |
| Open prospective study of low vitamin B12 levels not related to pernicious anemia (n = 30) | Oral crystalline cyanocobalamin: between 1000 and 125 μg/day, during the condition and continue at least 1 week | • Normalization of serum vitamin B12 levels in all patients with at least a dose of vitamin ≥250 μg/day  
• Dose effect–effectiveness dose of vitamin B12 ≥500 μg/day |
| Open prospective study of low vitamin B12 levels related to pernicious anemia (n = 10) | Oral crystalline cyanocobalamin: 1000 μg/day, during the condition and continue at least 3 months | • Significant increase of serum vitamin B12 levels in 90% of the patients (mean of 117.4 pg/mL)  
• Significant increase of Hb levels (mean of 2.45 g/dL) and decrease of MECV (mean of 10.4 fl) |

Hb: hemoglobin; MECV: mean erythrocyte cell volume.

Table 5. Study by our team on oral cobalamin therapy: Results on hematological manifestations [36].
for FCM and Biermer’s disease; and (2) thereafter, a weekly dose between 2000 and 1000 μg of vitamin B12 for FCM and a daily dose of 1000 μg (for all the life) in case of Biermer’s disease [37].

In vitamin B9 deficiency, therapeutic doses of vitamin B9 vary between 1 and 5 mg/day [38]. Usually, supplementation is continued for at least 3–6 months, provided that the underlying causes of the deficiencies have been corrected.

Food sources of nutrients are best for prevention of nutritional anemia, but often supplementation is necessary, especially for the elderly [39]. The USA National Academy of Sciences recommends that vitamin B9 and vitamin B12 standardized supplementation should be done (fortified cereal) in elderly.

11. Conclusions

In elderly patients, nutritional anemia represents 30–40% of all anemia. About two-third of this nutritional anemia is related to iron deficiency. Iron deficiency anemia is mainly the result of chronic blood loss from gastrointestinal lesions (with benign lesions in two-third of the cases). The remaining cases of nutritional anemia are usually associated with vitamin B12 and/or vitamin B9 deficiency. In elderly patients, vitamin B12 deficiency is most frequently related to food-cobalamin malabsorption; vitamin B9 is related to inadequate dietary intake or malnutrition, several drugs (as methotrexate, cotrimoxazole) and chronic alcohol intake. Treatment of nutritional anemia is simple and involves replacement of the deficient nutrient but requires particular attention to discerning the cause.

Conflict of interest

None related to the content of the present chapter.

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