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Original article

Anaemia in the elderly: An aetiologic profile of a prospective cohort of 95 hospitalised patients

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ABSTRACT

Background and objectives: Anaemia is a significant problem in the elderly, and the cause of anaemia in approximately one third of the general population is unidentified. To date, only a few studies have focused on hospitalised patients.
Patients and methods: We prospectively included anaemic patients (according to OMS criteria) aged 65 years and older who were hospitalised in the internal medicine department. The typical clinical data were collected, and a standardised set of biological tests, including cupraemia was performed.
Results: Of 360 total patients, 191 (53%) patients were anaemic; however, 96 patients were excluded because their data were incomplete. Of the remaining 95 patients that were included, 45 were men (47.4%) and 50 were women (52.6%); the mean patient age was 79.7 years (66–101 years). At least one cause of anaemia was diagnosed in 87 of the 95 (91.6%) patients, and anaemia was multifactorial in 44 of the 95 (46.3%) cases. The five most prominent causes of anaemia were inflammation (62.1%), iron deficiency (30.5%), folic acid deficiency (21%), chronic renal failure (17.9%) and cobalamin deficiency (11.6%). Microcytosis was present in only 27.5% of the patients who had an iron deficiency, and macrocytosis was present in only 7.4% of the patients who had a folic acid and/or cobalamin deficiency. The cause of anaemia could not be identified for 8 of the patients. The cupraemia was normal in all the patients.
Conclusion: A predefined protocol for older hospitalised patients was ability to identify the aetiology of anaemia in 91.6% of the cases; strikingly, anaemia was frequently caused by more than one factor (43.5%). Diagnostic orientation based on the mean corpuscular volume does not appear to correlate with mean cellular volume profile. Finally, anaemia caused by an unknown aetiology is rare and copper deficiency was not documented in any case.

1. Introduction

Anaemia is a significant problem in the elderly and has an estimated frequency of 10% in community dwelling populations that are older than age 65 [1,2]. This frequency can be as high as 40 to 60% in hospitalised patients or nursing home residents [3–5]. Anaemia, even of low degree (haemoglobin > 100 g/l), is an independent risk factor for mortality and is associated with decreased physical performance, an increased risk of physical weakness/falls and cognitive impairment [4–9]. The optimal haemoglobin correction is conditioned by the determination of anaemia's cause. However, the aetiology of anaemia remains unknown in approximately one third of all cases [1,10]. Previous studies that have reported a high incidence of anaemia of unknown origin were conducted in community dwelling populations. We evaluated the etiologic profile of anaemia and determined the frequency of anaemia with an unknown origin in hospitalised patients older than 65. We conducted a prospective monocentric study using a standardised set of exams. We also included a cupraemia assay in this set of exams to test the hypothesis that copper deficiency may play a role in anaemia of unknown origin in the elderly.

2. Patients and methods

We conducted a prospective study in the internal medicine department in a French general hospital (Hôpitaux Civils de Colmar) between March 1 and May 1, 2010.

2.1. Inclusion and exclusion criteria

The patients were included if they were 65 years or older and had anaemia. Anaemia was defined by the OMS criteria of a haemoglobin level <120 g/l in women and <130 g/l in men. Anaemia had to be present at admission and confirmed 48 h later. The exclusion criteria were anaemia caused by an acute bleeding, transfusion of red blood

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cells in the past seven days prior to admission or patients under palliative care.

2.2. Sample collection and data analysis

The main epidemiological and clinical data were collected, and a standardised set of biological tests was performed within 48 h after admission. The biological tests included a complete blood count with reticulocytes and red cells indices, C reactive protein, serum iron, serum transferrin, transferrin saturation, ferritin level, cobalamin (vitamin B12) and acid folic levels, renal function assessed by serum creatinine and calculation of the estimated glomerular filtration rate with the Modification of Diet in Renal Disease (MDRD) equation, serum protein electrophoresis, thyreostimulin hormone (TSH) and T4 thyroxin.

Cupraemia was also analysed for all of the patients. We hypothesised that a copper deficiency may explain some cases of unknown anaemia in the elderly because copper deficiency causes pseudo-myelodysplastic syndrome and is associated with malnutrition, which is common in the elderly [11].

Any additional analyses, including bone marrow examinations were performed at the discretion of the treating physician and the results were recorded during the study.

We analysed, when possible, the causes of inflammatory syndrome and iron and vitamin deficiencies.

2.3. Definition of anaemia categories

- Anaemia secondary to an iron deficiency was diagnosed if the serum iron level was <12 mg/l, the transferrin level was >2.9 g/l, the transferrin saturation was <20% and/or the ferritin level was <45 ng/ml [12].
- Anaemia secondary to a cobalamin deficiency was diagnosed if the serum level was <150 pmol/l [13].
- Anaemia secondary to an acid folic deficiency was diagnosed if the serum was level was <5 nmol/l [1].
- Anaemia secondary to a copper deficiency was considered if cupraemia was <10 μmol/l [11].
- Anaemia caused by inflammation was defined by a C reactive protein level >10 mg/l and a ferritin level >100 ng/ml [14].
- Anaemia considered secondary to renal insufficiency with a severe chronic renal dysfunction was defined by an EGFR <40 ml/min/1.73 m^2 according to the MDRD equation [15].
- Anaemia secondary to hypothyroidism was defined by a serum TSH level >10 UI/l and a serum T4 level <11 pmol/l [16].
- Anaemia secondary to other specific causes included: haematological malignancies, haemolysis, drug induced anaemia and hypersplenism of non-haematological aetiology.

We also analysed the cause of iron and vitamin deficiencies when possible.

The anaemia was considered multifactorial if at least two causes were identified (e.g., two different nutrient deficiencies).

It is difficult to diagnose mixed anaemia secondary to an iron deficiency and inflammation because there is no common definition. We arbitrarily diagnosed anaemia secondary to an iron deficiency and inflammation as a ferritin level <100 ng/ml in the context of an inflammatory syndrome, which was indicated by a C reactive protein concentration >10 mg/l [14,17]. If no cause could be identified, then the anaemia was classified as “unknown aetiology”.

3. Results

3.1. Study population

A total of 360 patients aged 65 years or older were hospitalised during the 2 month study period. Of these 360 total patients, 191 (53%) patients were anaemic. The proportion of anaemic women were 104/208 (50%) and the proportion of anaemic men were 87/152 (57%). Ninety-six anaemic patients were excluded from our study; three had bleeding at the time of admission, 3 received a red blood cell transfusion within 7 days of admission, 15 were under palliative care and 74 had incomplete data.

A total of 95 patients were included in our study, where 45 of the patients were men (47.4%) and 50 were women (52.6%). The mean patient age was 79.7 years (66–101), and all of the patients were Caucasian.

The reasons for patient hospitalisation were anaemia (10 of 95 patients, 11%), infectious disease (25/95, 26%), falls or malaises (14/95, 15%), cardio-vascular disease (12/95, 13%), arthralgias (9/95, 9%), changes in general status (7/95, 7%) and miscellaneous reasons (18/95, 19%).

The main clinical characteristics of anaemia are presented in Table 1. A majority of the patients (58/95, 61.1%) had mild anaemia with a haemoglobin level greater than 100 g/l. The haemoglobin level was between 80 and 100 g/l in 32 (33.7%) patients and was <80 g/l in 5 (5.2%) patients. The mean corpuscular volume was normal in 82.1% of the patients, and anaemia was non-regenerative in 96.8% of the patients.

3.2. Anaemia aetiology

At least one cause of anaemia was identified in 87 of the 95 (91.6%) patients, while multiple factors were identified in 44 (46.3%) of the cases.

The etiologic profile of anaemia is shown in Table 2.

Inflammatory anaemia was diagnosed in 59 (62.1%) of the 95 total patients, and the main cause of inflammation was acute infection (52.5%). In the remaining cases, inflammation was associated with cancer, chronic inflammatory disease or an unknown aetiology.

Iron deficiency was diagnosed in 29 (30.5%) of the patients. The cause of chronic blood loss was found in 20 of 29 cases; there were benign digestive lesions in 17 patients, colic adenocarcinoma in 1 patient, pelvic neoplasia in 1 patient and hereditary telangiectasias in 1 patient.

Mixed origin anaemia related to an inflammatory syndrome and iron deficiency was diagnosed in 22 of the patients (23%), and the cause of the chronic blood loss was identified in 13 of these 22 (59%) patients. The cause of the iron deficiency remained unknown for 9 patients because no digestive endoscopy was performed. All of these patients had an associated inflammatory syndrome.

A nutritional folate deficiency was diagnosed in 20 of the 95 (21%) anaemic patients and was associated with chronic ethylism in 3 cases.

Cobalamin deficiency was diagnosed in 11 (11.6%) of the 95 patients, which was caused by cobalamin nutritional malabsorption

Table 1
Main characteristics of anaemia in 95 hospitalised patients aged 65 years and older.

Haematological parameters	Mean values
Haemoglobin (g/l)	103 (60–129)
Haemoglobin (g/l) > 100 n (%)	58 (61.1)
Haemoglobin (g/l): 80–100 n (%)	32 (33.7)
Haemoglobin (g/l) < 80 n (%)	5 (5.2)
VGM (fl)	90.2 (62.1–110)
Microcytic anaemia VGM < 80 fl n (%)	9 (9.5)
Macrocytic anaemia VGM > 100 fl n (%)	8 (8.4)
Normocytic anaemia VGM 80–100 fl n (%)	78 (82.1)
Reticulocytes < 120,000/mm^3 n (%)	92 (96.8)