Ann Hematol (2001) 80:295–298
DOI 10.1007/s002770100287

ORIGINAL ARTICLE

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Anemia: an indicator for malnutrition in the elderly

Received: 11 July 2000 / Accepted: 19 December 2000 / Published online: 6 March 2001

Abstract The prevalence of anemia increases with age and is frequently multifactorial. We postulated that malnutrition contributes to anemia in the elderly and is underdiagnosed. Our objective was to analyze the prevalence of anemia and its association with nutritional status in a hospitalized geriatric population. Included in this retrospective cohort study were 186 consecutive patients admitted in 1997 to a geriatric unit of a university hospital. We compared hematological and chemical blood tests routinely performed upon admission in patients with anemia (hemoglobin <120 g/l) and without anemia (hemoglobin ≥120 g/l). Using these admission parameters, we defined a multiparameter score of malnutrition by low lymphocyte counts, decreased values of albumin, cholesterol, transferrin, cholinesterase, and zinc, iron deficiency by low transferrin saturation and normal C-reactive protein, and inflammation by increased C-reactive protein and high transferrin saturation. Of the 186 patients, 82 (44%) met the criteria for anemia on admission. In univariate analysis, patients with anemia differed significantly from patients with normal hemoglobin exhibiting lower serum values of albumin, iron, transferrin, cholesterol, cholinesterase, zinc, transferrin saturation, and lymphocyte count and higher C-reactive protein levels. Using a multiparameter score, anemia correlated significantly with parameters of malnutrition (P=0.0001) but not with iron deficiency (P=0.5) or with inflammation (P=0.08). In a multivariate logistic regression model, anemia was significantly associated with serum albumin (RR: 1.138; 95% CI: 1.056–1.227; P=0.0007), cholinesterase (RR: 1.387; 95% CI 1.122–1.714; P=0.0025), and transferrin saturation (RR: 1.05; 95% CI: 1.012–1.09; P=0.009). We conclude that malnutrition may play an important etiologic role in anemia in the elderly.

Keywords Anemia · Age · Geriatric · Malnutrition · Iron deficiency · Anemia of chronic disease

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Introduction

Anemia is common in the elderly [1]. A high prevalence of anemia is observed in hospitalized or institutionalized older individuals [5, 7, 9, 14]. In contrast to younger adults, anemia in this cohort of patients is frequently multifactorial. Bleeding, resulting in iron deficiency, and chronic disease such as infections and malignancy play an important role. Malnutrition as a contributing factor is probably underestimated. Evidence of malnutrition is found frequently in hospitalized elderly patients [11, 12, 13]. Parameters such as serum albumin, transferrin, transferrin saturation, cholesterol, cholinesterase, vitamin B_{12}, folic acid, zinc, and absolute lymphocyte count are useful to assess the nutritional status. The aim of this study was to evaluate the prevalence of anemia in patients admitted to a geriatric ward and to assess the influence of malnutrition as a contributing factor and its relationship with iron deficiency and inflammation.

Patients and methods

Patients

We retrospectively reviewed records of all admissions to the Basel Geriatric University Clinic in 1997. This is one of three geriatric hospitals in the city. Patients are admitted to any of these institutions by availability of beds, and patients admitted to our hospital are likely to be representative of the Basel hospitalized geriatric population. We recorded the patient's age, sex, date of admission and discharge, place of residence (home or other institution such as nursing home or hospital), place of discharge (home, other institution), and mortality. Underlying disease and reason for admis-

sion were categorized as well as two secondary diagnoses if relevant for the development of anemia or malnutrition. Categories of reason for admission considered were (1) falls, (2) confusion, (3) acute illness, or (4) loss of independence in activities of daily living (IADL). Underlying disease was categorized as (1) infection or malignancy, (2) acute illness other than infection or malignancy, or (3) other chronic conditions or loss of IADL. Prior to admission, 80% of the patients resided at home. Most of them were admitted via the emergency room.

In 1997 there were 196 admissions. For patients with repeated admissions, only the first admission was considered. This study included 186 patients: five repeated admissions and five patients with missing data were excluded. Their median age was 85 years. According to the inclusion criteria, four patients younger than 65, the age limit usually set for old age, but with conditions typical for a geriatric population such as presenile dementia were included in the analysis. Patients with chronic disease and malignancy were not known to have bone marrow infiltration by a malignant process except for three patients with previously diagnosed myelodysplastic syndrome.

Upon admission to the geriatric ward, hematological and chemical blood values were measured in all patients. Blood samples were drawn in the morning following admission prior to breakfast. The following parameters were considered for this study: differential blood counts, albumin, ASAT, ALAT, cholesterol, C-reactive protein, iron, transferrin, transferrin saturation, vitamin B_{12}, folic acid, cholinesterase, zinc, and thyroid-stimulating hormone (TSH). Folic acid was measured as either serum folic acid or as erythrocyte folic acid. Ferritin was not routinely included in the admission work-up and was therefore assessed in only half the patients.

Study design and definitions

We tried to characterize anemia using hematological and chemical blood values determined systematically at the time of the patient's admission to hospital. Therefore, the patients were grouped according to their hemoglobin values into those with anemia (<120 g/l) and those without (≥120 g/l). All hematological and chemical blood values were then compared by univariate and multivariate analysis. In a second step, we tried to establish scores suggesting malnutrition, iron deficiency, and chronic disease. Biochemical evidence of malnutrition was considered to be present if ≥5 of the following criteria were met: serum albumin <35 g/l (reference range: 35–52 g/l), absolute lymphocyte count $<1.5\times10^9$/l ($1.6–2.4\times10^9$/l), cholesterol <3.0 mmol/l (3.0–5.2 mmol/l), transferrin <2 g/l (2.0–3.6 g/l), cholinesterase <7.0 IU/ml (7.0–19.0 IU/ml), zinc <10.7 µmol/l (10.7–22.9 µmol/l). Iron deficiency was defined as transferrin saturation below 15% (16–45%) with normal CRP (<5 mg/dl). Biochemical evidence of inflammation was considered to be present if all three of the following criteria were met: C-reactive protein higher than 5 mg/dl, transferrin saturation higher than 15%, and serum iron levels below 9.5 µmol/l (9.5–33.8 µmol/l).

Statistics

The results are presented as medians and ranges. Pearson's chi-squared test was used for group differences with categorical variables and the Mann-Whitney U test for differences with continuous variables. Univariate estimation of the association of anemia with malnutrition, iron deficiency, and inflammation was done with Pearson's chi-squared test. A multivariate logistic regression model with stepwise variable entry was used to determine which factors were significantly associated with anemia. *P* values <0.05 were considered significant. Statistical analysis was performed using the SPSS statistical program (SPSS for Windows, release 9.0, SPSS, Chicago, Ill., USA).

Results

Of the 186 patients included in this study, 82 (44%) fulfilled the criteria for anemia, and 104 did not have anemia. The median age of the entire cohort was 85 years (range: 56–100); 93 (50%) were male. There were no significant differences among patients with and without anemia with respect to age, gender, duration of hospitalization, reason for admission, primary diagnosis, place of residence prior to admission, and place of discharge (Table 1).

Table 1 Patients' characteristics

	All patients	Anemia	No anemia	*P*
n	186	82	104	
Sex: female (*n*,%)	93 (50%)	42 (51%)	51 (49%)	0.8
Median age in years (range)	85 (56–100)	84 (56–97)	85 (85–100)	0.4
Median days in hospital (range)	43 (1–442)	42 (2–442)	46 (1–424)	0.8
Reason for admission				0.1
Falls	51 (27.4%)	24 (29.3%)	27 (26%)	
Confusion	22 (11.8%)	5 (6%)	17 (16.4%)	
Acute illness	64 (34.4%)	27 (33%)	37 (35.6%)	
Loss of IADL	49 (26.3%)	26 (31.7%)	23 (22%)	
Main diagnosis				0.8
Infection/malignancy	52 (28%)	24 (29.3%)	28 (27%)	
Acute illness other than infection or malignancy	50 (26.9%)	23 (28%)	27 (26%)	
Other chronic conditions or loss of IADL	84 (45.2%)	35 (42.7%)	49 (47%)	
Admission from				0.1
Home	148 (79.6%)	61 (74%)	87 (84%)	
Other institution	38 (20.4%)	21 (26%)	17 (16%)	
Discharge				0.5
Home	62 (33.3%)	24 (29.3%)	38 (36.5%)	
Other institution	67 (36%)	30 (36.5%)	37 (35.6%)	
Death	57 (30.6%)	28 (34.1%)	29 (27.9%)	

IADL independent activities of daily living

Table 2 Admission parameters (medians and ranges) for all patients as well as according to hemoglobin value

Parameter	Reference values	*n*	All patients (*n*=186)	Anemia (*n*=82)	No anemia (*n*=104)	*P*
Hemoglobin	120–160 g/l	186	126 (73–174)	106 (73–119)	138 (120–174)	
MCV	79.0–95.0 fl	186	91.9 (64.1–116.3)	92 (77–116.3)	91.7 (64.1–112)	0.8
MCH	27.0–31.0 pg	186	29.7 (19.4–36.8)	29.2 (22.4–35.2)	29.9 (19.4–36.8)	0.1
Platelet count	150–450×10^9/l	186	249 (10–903)	255 (10–774)	244 (112–903)	0.4
Leukocytes	3.5–10×10^9/l	186	7.65 (1.46–38.05)	7.69 (1.46–38.05)	7.63 (3.64–21.70)	0.4
Lymphocytes	1.6–2.4×10^9/L	180	1.16 (0.01–16.86)	1.04 (0.06–16.86)	1.31 (0.01–7.95)	0.01
Iron	9.5–33.8 µmol/l	186	8.80 (1.5–45.1)	6.4 (1.5–35.4)	10.15 (1.8–45.1)	<0.001
Transferrin	2.00–3.60 g/l	186	2.14 (0.71–4.95)	2.01 (0.71–4.16)	2.33 (1.17–4.95)	<0.001
Transferrin saturation	16–45%	186	16 (3–87)	14 (3–56)	17 (4–87)	0.003
Ferritin	15–300 pmol/l	89	250 (26–8280)	302 (32–8280)	208 (26–2656)	0.9
Folic acid[a]		177				
Serum	7–39 nmol/l	55	10 (4–45)	11 (4–45)	10 (4–45)	0.7
Erythrocyte	395–1585 nmol/l	122	700 (145–2953)	741 (300–2953)	685 (145–2250)	0.4
Vitamin B_{12}	132–835 pmol/l	180	235 (47–3260)	262 (69–1730)	221 (47–3260)	0.06
Albumin	35–52 g/l	185	34 (15–48)	31 (15–46)	36 (22–48)	<0.001
Cholesterol	3.0–5.2 mmol/l	183	4.66 (1.67–11)	4.37 (2.05–11)	5.03 (1.67–9.39)	<0.001
Cholinesterase	7.0–19.0 IU/ml	178	7.5 (1.9–15.8)	6.1 (1.9–11.0)	8.2 (4.2–15.8)	<0.001
CRP	<5 mg/l	185	23 (<5–398)	35 (<5–304)	19 (<5–398)	0.03
ASAT	11–36 U/l	185	27 (9–530)	26 (9–185)	28 (10–530)	0.5
ALAT	10–37 U/l	185	19 (2–480)	19 (2–480)	19 (5–135)	0.5
TSH	0.1–4.0 mIU/l	178	1.29 (0.01–75.3)	1.23 (0.01–38.4)	1.36 (0.07–75.3)	0.7
Zinc	10.7–22.9 µmol/l	169	10.0 (4.2–15.9)	9.6 (4.2–15.4)	10.6 (4.2–15.9)	0.04

[a] Folic acid was measured as either serum or erythrocyte folic acid

Table 3 Prevalence of malnutrition, iron deficiency, and inflammation in elderly patients with and without anemia

Scores of	Anemia (*n*=82)	No anemia (*n*=104)	*P*
Inflammation	14 (17%)	9 (9%)	0.08
Iron deficiency	4 (5%)	8 (8%)	0.5
Malnutrition	34 (42%)	12 (12%)	<0.001
Neither	30 (36%)	75 (72%)	<0.001

The results of the hematological and chemical blood values for all patients determined upon hospitalization as well as stratified according to hemoglobin are shown in Table 2. Complete blood counts and biochemical parameters were available in >90% of the patients, except for ferritin. Patients with anemia had significantly lower lymphocyte counts, serum iron, transferrin levels, transferrin saturation, albumin, cholesterol, cholinesterase, and zinc, but higher C-reactive protein (Table 2). There were no differences for the other parameters: leukocyte count, platelet count, vitamin B_{12}, folic acid, ASAT, ALAT, and TSH.

Of 82 of the patients with anemia, 34 (42%) met the criteria for malnutrition as compared to 12 of 104 (12%) of the patients without anemia (P<0.0001). A low transferrin saturation in the presence of a normal CRP suggesting iron deficiency was found in 4 of 82 (5%) of the patients with anemia and in 8 of 104 (8%) of those without anemia (P=0.5). A positive inflammation score was found in 14 of 82 (17%) and 9 of 104 (9%; P=0.08), respectively (Table 3). In a multivariate logistic regression model, anemia was significantly associated with low serum albumin (RR: 1.138; 95% CI: 1.056–1.227; P=0.0007), with decreased transferrin saturation (RR: 1.05; 95% CI: 1.012–1.09; P=0.009), and with low cholinesterase (RR: 1.387; 95% CI 1.122–1.714; P=0.0025). The relative risk of the association of anemia with serum albumin of 1.138 is best interpreted as an increase in the probability of having anemia by 14% with every decrease of serum albumin by 1 g/l. Relative risks of transferrin saturation are by saturation percent and for cholinesterase by IU/ml.

Discussion

In this retrospective cohort study analyzing 186 consecutive admissions to a geriatric ward in a university hospital, we found a high prevalence of anemia of 44%. Patients with anemia had significantly lower serum concentrations of albumin, iron, transferrin, cholesterol, cholinesterase, and zinc, a lower transferrin saturation, and a higher C-reactive protein level. Using a multiparameter score, anemia was significantly associated with parameters related with malnutrition (P=0.0001) but not with inflammation (P=0.08) or iron deficiency (P=0.5). In a multivariate logistic regression model, only serum albumin, cholinesterase and transferrin saturation, all markers of malnutrition, were associated with anemia.

Multimorbidity in the elderly makes causal diagnosis of anemia difficult [3, 4, 6, 10, 14]. Multiple factors such as vitamin and iron deficiency, chronic bleeding, and chronic infectious, inflammatory, and malignant conditions may coexist. Furthermore, laboratory tests such as ferritin may be misinterpreted in cases of concomitant inflammatory states. The data presented show that parameters of malnutrition are strongly associated with anemia and suggest that malnutrition contributes to the development of anemia in these patients. In the multivariate model, only serum albumin and cholinesterase, both

reflecting nutritional status, and transferrin saturation, reflecting nutritional status and iron body stores, were significantly associated with anemia. As the socioeconomic status of the elderly in Switzerland is high and poverty has become rare, malnutrition more likely reflects loneliness and depression, poor dentition, loss of appetite, impairment of cognitive function, or secondary systemic disease. As shown in Table 1, patients with anemia did not differ from patients with normal hemoglobin in the distribution of underlying diseases. It is notable that blood vitamin levels such as B_{12} and folic acid were not different in patients with or without anemia. These data are difficult to interpret and may reflect the attention given to early substitution as outpatients.

Anemia may contribute to reduced quality of life in the elderly, may predispose to falls and its consequences such as fractures, and may further impair cognitive function [2]. In this study, we found no significant difference in hospital mortality or place of discharge between patients with and without anemia. Nevertheless, the high prevalence of anemia and the strong association with nutritional status is disturbing.

This study has several limitations. The population analyzed is small but likely to be representative for a hospitalized geriatric population in this region with high socioeconomic standard. The main finding, an association of anemia with markers of malnutrition, is significant in spite of the small sample size. The definitions of anemia, malnutrition, iron deficiency, and chronic inflammation used are based on the availability of the routine profile on admission and are therefore somewhat arbitrary and certainly open to criticism. Ferritin levels were not determined in half the patients, and therefore the definition of iron deficiency is uncertain. Using these definitions, we are probably underestimating rather than overestimating the impact of iron deficiency. The lack of association of anemia with the reason for admission, underlying disease, or sex may be due to sample size restriction. The parameters analyzed are not disease specific, and conditions such as hypoalbuminemia may indicate malnutrition as well as chronic disease. We had body weight data available but no reliable measures of body height in this group due to kyphosis etc. and thus no estimation of the body mass index. We also lack data on nutritional intake in these patients. However, the association of anemia with multiple markers of malnutrition makes our interpretation plausible.

In conclusion, we found a high prevalence of anemia in a geriatric population upon admission to the hospital. Anemia is probably multifactorial; however, malnutrition seems to play an important role and may be underestimated. It remains to be determined whether this nutritional component of anemia is amenable to intervention through better attention to nutritional status and whether this will benefit the patient. Results of this observational study should be interpreted cautiously but may serve to generate hypotheses to be tested in a prospective trial.

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