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Review

Anaemia in the elderly☆

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ABSTRACT

Anaemia is common in the elderly and is associated with an increased risk of physical, functional, and cognitive impairment, hospitalization and mortality. Although it is unknown whether anaemia is a causal factor or a subrogated marker of worse health status, its correction can improve the patients' physical and functional capacity. Detection, classification, and treatment of anaemia should be a priority for the health system. The main causes of anaemia in the elderly are nutritional deficiencies and chronic disease, with or without kidney failure, although some cases are of indeterminate origin. Medical history and physical examination help to clarify its aetiology. A diagnostic algorithm based on data from the lab allows anaemia classification with a therapeutic orientation. Supplements of iron and maturation factors, as well as erythropoiesis-stimulating agents, constitute the mainstay of treatment, along with that of the underlying disease, whereas red blood cell transfusion should be reserved for severe cases.

La anemia del anciano

Palabras clave:
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RESUMEN

La anemia es frecuente en los ancianos y se asocia con un mayor riesgo de deterioro físico, funcional y cognitivo, hospitalización y mortalidad. Aunque desconocemos si es un factor causal o un marcador subrogado de un peor estado de salud, su corrección puede mejorar la capacidad física y funcional. Su detección, su clasificación y su tratamiento deberían ser objetivos prioritarios para el sistema de salud. Sus principales causas son las deficiencias nutricionales y las enfermedades crónicas, con y sin insuficiencia renal, aunque algunas son de origen desconocido. La historia clínica y la exploración física ayudan a aclarar su etiología. Un algoritmo diagnóstico basado en los datos del laboratorio permite su clasificación con orientación terapéutica. Los suplementos de hierro y factores madurativos y los agentes estimuladores de la eritropoyesis constituyen la base del tratamiento, junto con el de la enfermedad de base, reservándose la transfusión de hematíes para los casos graves.

> Growing old is like climbing a great mountain. While you climb, your strength grows weak, but the gaze is freer, the view more clear and serene
>
> INGMAR BERGMAN

Introduction

The average life expectancy has increased drastically over the last century (from ≈60 years in 1900 to ≈80 years in 2015) and is estimated to increase further in the future.[1] In the European Union, the proportion of individuals ≥80 years will triple between 2011 and 2060.[2] With age there is an inevitable deterioration of the organic functionality (ageing) that eventually leads to death. Age is also a risk factor for common processes, whether diagnosed or not, such as cardiovascular disease, cancer, diabetes or Alzheimer's disease, which increase the risk of mortality.[1]

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Factors responsible for the phenotypic changes leading to the loss of physiological reserve, organic failure and reduction of the functionality have a role in the ageing process. The sum of these factors would give rise to the clinical features in the elderly: frailty, anaemia, malnutrition and poor immune response.[1] Whether anaemia is an independent risk factor for functional impairment, a surrogate marker of a worse health status or simply an additional comorbidity, is something that we still do not know.

A better understanding of the molecular basis of ageing would facilitate the development of interventions that, if applied early, could prevent, delay, alleviate or even reverse some of the diseases related to ageing, thereby gaining years of independent living. That is, we would not only add "years to life", but also "life to years".

Definition and prevalence of anaemia in the elderly

According to the World Health Organization (WHO), the concentration of haemoglobin (Hb) that defines the presence of anaemia in the elderly would be <13 g/dl in men and <12 g/dl in women.[3] With these definitions, between 1993 and 2005 anaemia affected 24% of the world's elderly (164 million individuals), although with important regional differences.[4] However, there are authors who question its validity in the elderly, in whom an Hb value near the lower limit of normality could be associated with a worse physical and cognitive state.[5]

At the *Third US National Health and Nutrition Examination Survey* (NHANES III, Phases 1 and 2, 1988–1994; 26,372 individuals), the prevalence of anaemia in individuals ≥65 years of age progressively increased with age (13% in individuals aged 75–84 years, 23% in the 85 years old or more) and was higher among men.[6] In the recent EMPIRE study in Portugal, the prevalence in 1617 individuals >65 years old was also higher in men (22.2%) than in women (19.9%) and increased with age (17.3% in 65–79 years, 31.4% in ≥80 years).[7]

The different prevalence of anaemia according to sex may reflect differences in incidence. In an elderly population of Olmsted County (Minnesota) = 618, the annual incidence increased with age and was higher in men (90.3 per 1000) than in women (69.1 per 1000).[8] In 465 cases (75%) anaemia was detected during hospital admission, although anaemia was the cause of hospitalization in only 57 cases.[8] In contrast, in the region of Piedmont (Italy) = 529, the annual incidence of anaemia and mild anaemia were 24.2 and 22.5 per 1000, respectively, with no differences between sexes, but increasing with age (4.9 per 1000 in the 65–69 years group, 72.4 per 1000 in the 80–84 years group).[9]

In a meta-analysis of 34 epidemiological studies (85,409 elderly), the mean prevalence was 17%, but fell to 6% when anaemia was defined by an Hb < 11 g/dl, indicating that it was mild in most cases. The prevalence was lower among the elderly living in the community (12%) than those living in nursing homes (47%) or that were hospitalized (40%).[10] In the InCHIANTI study, the prevalence of anaemia in the Italian population >65 years of age was 11%, rising to 48–60% in hospitalized individuals.[11] In a series of >300,000 elderly males admitted for non-cardiac surgery in the United States, 43% had a haematocrit <39%, but only <33% in 15% of cases, again indicating that anaemia was mild in most cases.[12]

In Spain, a multicenter study revealed that the prevalence of anaemia in elderly who had undergone surgery = 1687 ranged from 14% in prostate surgery to 61% in colorectal cancer.[13] Among non-operated hospitalized patients (n = 796) the mean prevalence was 57% (32% mild, 20% moderate, 5% severe), although there were differences according to the department.[14] Among the outpatient population, a study in the Huesca Sector (n = 32,666; 2011–2015) found that the prevalence of anaemia increased with age from 80 years onwards, being higher in men (16 and 12% among the 80–89 years old; 31.6 and 22.4% in >90 years old).[15] The total Spanish population will decrease from 46,507,760 in 2014 to 45,484,908 in 2029, while the population ≥65 years of age will grow from 8,442,887 (18.2%) to 11,275,805 (24.8%) (www.ine.es/prensa/prensa.htm). Extrapolating data from these studies, the number of anaemic elderly will increase from 1100,000 in 2014 to 1500,000 in 2029 (+36%), which will be a significant burden on our health system.

Consequences of anaemia in the elderly

Anaemia reduces physical capacity and muscle strength in the elderly, decreasing mobility and quality of life.[16] In addition, it increases the risk of fatigue, depression, dementia, hospitalization (due to exacerbations of intercurrent disease, falls) or admission to nursing homes (due to exacerbation of functional deterioration) and mortality (especially if accompanied by other disorders such as heart or kidney failure, high blood pressure or diabetes).[17,18] In a meta-analysis of 24 studies (949,445 patients), preoperative anaemia (39%) showed an independent association with an increased risk of transfusion, postoperative complications and mortality.[19] For this reason, the detection, classification and treatment of anaemia in the elderly should be a priority objective for the health system.

Hematin deficiencies without anaemia can also have consequences in the elderly. Individuals with hematinic deficiency without anaemia may develop symptoms such as fatigue or decreased exercise tolerance.[20] In congestive heart failure, iron deficiency is associated with decreased physical performance and quality of life and with increased mortality.[21] Iron deficiency can cause secondary thrombocytosis in renal failure, cancer or inflammatory bowel disease, increasing the risk of thromboembolic phenomena.[22] Generally, preclinical or moderate vitamin B deficiency[12] (5–20% of the elderly population) is not accompanied by anaemia but may contribute to cognitive impairment and increased thrombotic risk.[23,24]

Causes of anaemia in the elderly

Anaemia in the elderly usually has a multifactorial origin; all pathophysiological mechanisms are possible and many of them are simultaneous. In the NAHNES III study, nutritional deficiencies were responsible for 34% of the cases, while chronic diseases, with and without renal failure, accounted for another 33%.[7] In 33% of cases, it was not possible to identify the aetiology (unexplained anaemia in the elderly [UAE]).[7] The high prevalence of UAE (25–45%) in large epidemiological studies on thousands of individuals could simply reflect the use of a limited number of diagnostic tests.[17] When exhaustive studies (necessarily with much fewer cases) are carried out, only 15% of the anaemias are classified as UAE.[25]

Nutrient deficiency

Erythropoiesis needs about 20–25 mg of *iron* per day, 99% of which comes from Hb recycling of red blood cells in macrophages. Intestinal absorption only contributes 1% and compensates the daily losses. When the absorption decreases or the losses increase (Table 1A), iron deposits are used, decreasing progressively. This causes a progressive iron deficiency and finally iron deficiency anaemia (IDA), when enough iron is not available to synthesize Hb.[26,27]

Vitamin B_{12} is essential to produce red blood cells and the functioning of the nervous system. Its absorption depends on the intrinsic factor (synthesized by the gastric parietal cells), and is produced by the "cubam receptor" of the distal ileum. Decreased