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REVIEW

The impact of anaemia and iron deficiency in chronic obstructive pulmonary disease: A clinical overview

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Abstract
Introduction: Anaemia is increasingly recognised as an important comorbidity in the context of chronic obstructive pulmonary disease (COPD), but remains undervalued in clinical practice. This review aims to characterise the impact of anaemia and iron deficiency in COPD.
Methods: Literature review of studies exploring the relationship between anaemia/iron deficiency and COPD, based on targeted MEDLINE and Google Scholar queries.
Results: The reported prevalence of anaemia in COPD patients, ranging from 4.9% to 38.0%, has been highly variable, due to different characteristics of study populations and lack of a consensus on the definition of anaemia. Inflammatory processes seem to play an important role in the development of anaemia, but other causes (including nutritional deficiencies) should not be excluded from consideration. Anaemia in COPD has been associated with increased morbidity, mortality, and overall reduced quality of life. The impact of iron deficiency, irrespective of anaemia, is not as well studied, but it might have important implications, since it impacts production of red blood cells and respiratory enzymes. Treatment of anaemia/iron deficiency in COPD remains poorly studied, but it appears reasonable to assume that COPD patients should at least receive the same type of treatment as other patients.
Conclusions: Anaemia and iron deficiency continue to be undervalued in most COPD clinical settings, despite affecting up to one-third of patients and having negative impact on prognosis. Special efforts should be made to improve clinical management of anaemia and iron deficiency in COPD patients as a means of achieving better patient care.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a highly debilitating and life-threatening condition characterised by an airflow limitation that is not fully reversible, is generally progressive, and associated with enhanced inflammatory response in the lungs and airways.[1] COPD is associated with a variety of comorbidities that aggravate the overall prognosis, including cardiovascular, metabolic, pulmonary, and hematologic disease, as well as gastrointestinal and psychiatric disorders.[2,3]

The exact prevalence of COPD in most regions of the world is not known. Global prevalence has been estimated at 10.1% (11.8% for men and 8.5% for women),[4] but prevalence reports vary widely according to region and population under study.[1,5] In Portugal, specifically in the Lisbon area, Bárbara et al.[6] have previously identified a prevalence of 14.7%. COPD is generally more prevalent among smokers, men, and older individuals.[1] In many countries, the disease remains, however, vastly under-recognised and underdiagnosed since patients do not present until later stages of the disease, which is then reflected in prevalence and mortality estimates.[1] In this context, COPD is still the third leading cause of death in Europe and is estimated to become the third leading cause of death worldwide by 2020.[1] The increasing impact of COPD is mainly explained by past rates of smoking and the ageing population. The disease is expected to have major implications for quality of life and mortality, and will represent a considerable socio-economic burden over the next decades.[1]

A variety of systemic manifestations of COPD have been identified over the years. Recently, these have begun to be more closely studied to establish if there are significant underlying comorbid interactions impacting on the overall prognosis of COPD patients. Several comorbidities were found to impact on COPD prognosis, including heart failure, ischaemic heart disease, metabolic syndrome, pulmonary hypertension, anxiety and depression disorders, lung cancer, pulmonary fibrosis, osteoporosis, anaemia, gastro-esophageal reflux disease and peptic ulcer disease, chronic kidney disease, malnutrition, and sleep disorders.[2,3,7,8]

Anaemia is increasingly recognised as an important comorbidity in the context of COPD, affecting a relevant number of patients and with established negative impact on overall prognosis. There are several disease mechanisms which could potentially explain the increased occurrence of anaemia in COPD patients, including iron deficiency and inflammatory processes. Nonetheless, evidence about the role of anaemia, iron deficiency, and iron deficiency anaemia in the COPD patient remains limited and, consequently, these conditions continue to be undervalued in most COPD clinical settings.

This review aims to provide a clinical overview of the impact of anaemia and iron deficiency in COPD, including the proposed mechanisms of disease, clinical consequences, and potential effects of different treatment strategies.

Methods

In order to characterise the impact of anaemia and iron deficiency among COPD patients, we ran query on two electronic databases: MEDLINE via PubMed and Google Scholar. MEDLINE was selected because it is one of the most important aggregators of medical research reports worldwide. In addition, Google Scholar was also used to ensure that relevant research reports published in non-indexed journals were taken into consideration.

Both these databases were queried for clinical research reports published up till June 2016. The following search terms were used: ''Anaemia'', ''Anemia'', ''COPD'', ''Chronic obstructive pulmonary disease''; ''Chronic bronchitis''; ''Emphysema''; ''Iron deficiency''; ''Iron deficiency anaemia''; ''Iron deficiency anemia''. Search results were initially scanned based on title and abstract and, in cases where this initial assessment was not sufficient, article full-texts were also reviewed.

The search results yielded several systematic reviews on specific aspects of the relationship between COPD and anaemia, but these reviews also had substantial limitations due to the underlying variability of study design and population. In this review we do not present systematic data, such as a summary table with all study results, because this information is already available elsewhere in reasonable updated publications. Instead, in this clinical overview, we aim to provide a more straightforward review of the evidence on the impact of anaemia in the COPD patient, highlighting the implications for clinical practice. In addition, we also explore in greater detail the impact of iron deficiency alone or in the form of iron deficiency anaemia in the COPD patient.

Results

Prevalence of anaemia in COPD

The reported prevalence of anaemia in COPD patients has been highly variable, mostly due to the different characteristics of study populations and the lack of a consensus definition of anaemia in the context of COPD, which led to remarkably different estimates between studies.

In a 2011 systematic review, Yohannes et al.[9] identified 7 individual studies reporting the prevalence of anaemia in COPD populations and found an overall prevalence of anaemia ranging from 7.5% to 32.7%. Most studies consisted of retrospective assessments of medical records, with no standardised anaemia definition and evaluating notably different—and virtually incomparable—COPD populations, which explains this variability in prevalence estimates.

Two further updated reviews, conducted in 2015, identified 24 studies reporting on the prevalence of anaemia in COPD.[10,11] These reviews encountered, nonetheless, the same issues highlighted in the initial systematic review, and further extended the range of prevalence from 4.9% to 38.0%.[10,11] Variations in the prevalence of anaemia between different studies were attributed to both the intrinsic characteristics of each study population and the different definitions of anaemia—and even COPD diagnosis—applied throughout the studies.[10] The definitions of anaemia varied substantially across different studies; while most authors used the World Health Organisation (WHO) definition, some used the same haemoglobin level for both men and women (since most women were post-menopausal) and others used

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