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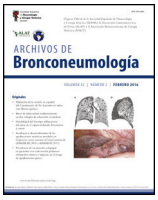

Editorial

GesEPOC 2021: One More Step Towards Personalized Treatment of COPD☆

GesEPOC 2021: un paso más en la personalización del tratamiento de la EPOC

The first edition of the Spanish COPD Guidelines (GesEPOC) changed the approach to the medical treatment of COPD. For the first time, the concept of clinical phenotype was included to guide more personalized treatment.[1] In the 10 years since the publication of that initial document, several studies have validated the classifications proposed in these guidelines,[2–4] and we have witnessed the progressive implementation of the GesEPOC guidelines at all levels of care.[5,6] However, one of the important features of these guidelines is that they must constantly be updated as new evidence emerges, and for this reason the GesEPOC working group has begun work on a new version for 2021. This new edition will retain the major conclusions that have already been validated,[2–4] but it will address changes emerging from the outcomes of recent studies. We should emphasize that the content of this editorial reflects the opinions of the authors and not necessarily the opinions of the GesCOPD group, and we stress that these issues are still under discussion. This sole purpose of this editorial is to summarize some of the most novel aspects that will be addressed in the development of the new guidelines.

One topical issue is the indication for triple therapy (long-acting beta agonists [LABA], long-acting muscarinic antagonists [LAMA], and inhaled corticosteroids [ICS]) in COPD, and more particularly, what is the benefit of (and who will benefit from) adding an ICS to the LABA/LAMA combination.[7] This question has been addressed in the recent American Thoracic Society (ATS) guidelines,[8] and it appears that response depends on several factors, including the concentration of eosinophils in blood, the frequency and severity of exacerbations, and active smoking.[8,9] In any case, evidence that the efficacy of ICS gradually increases as blood eosinophil concentration rises is increasingly convincing.[10] However, the use of peripheral eosinophilia as a marker involves a number of difficulties arising from the need to establish thresholds for the indication (or withdrawal) of ICS, its variability, the moment when the determination should be made, the number of determinations needed, and their frequency. These issues have not yet been completely resolved, but several proposals have reached a broad consensus, especially regarding the greater efficacy of ICS in patients with eosinophils >300 cells/mL and the lack of efficacy when eosinophils are <100 cells/mL; however; agreement on the use of ICS in patients with eosinophils between 100 and 300 cells/mL,[9] constituting a very large group of COPD patients, is much lower.[11]

The existing evidence shows that classifying patients by their blood eosinophilia levels may be more useful in clinical terms than the traditional phenotypes of chronic bronchitis and emphysema. With the exception of roflumilast, the use of which is very limited, none of the medical treatments approved for COPD depend on these phenotypes for their indication. Peripheral eosinophilia has also been included in a recent European Respiratory Society (ERS) guideline on ICS withdrawal,[12] and this marker is becoming increasingly established as a valid and necessary tool in clinical practice. GesEPOC was an early advocate of the use of eosinophilia to guide the treatment of COPD, and included this approach in the first definition of asthma-COPD overlap (ACO) that appeared in the 2012 GesEPOC.[1] The 2021 document introduces the concept of treatable traits, such as frequent exacerbations or peripheral eosinophilia, and the classic phenotypes of emphysema and chronic bronchitis can be also classified as phenotypic treatable traits. It is useful to identify emphysema so that endoscopic volume reduction techniques may be indicated, and chronic bronchitis may alert the clinician to the presence of bronchiectasis and chronic bronchial infection, but neither phenotype is associated *per se* with a specific drug treatment. Other treatable traits in COPD may include pulmonary hypertension, respiratory failure, or chronic bronchial infection, to name but a few.[13]

Eosinophilic COPD is a concept that may replace asthma-COPD overlap (ACO). Eosinophilia is one of the key factors in the definition of ACO in the Spanish consensus[14] and this eosinophilia is the characteristic that determines the diagnosis of ACO in most patients.[15] To avoid confusion, patients with a past or current diagnosis of asthma should be excluded from the GesEPOC guidelines, meaning that patients with eosinophilic COPD would be the only ACO patients specified in the guidelines.

An important treatment-related issue is the need to improve assessment of patient outcomes during follow-up. In contrast to asthma, there is currently no commonly used tool for evaluating adequate control of COPD. For this reason, a brief COPD control questionnaire has been developed and validated. This instrument includes questions about clinical status and allows patients to be classified as controlled or uncontrolled, with important short- and long-term prognostic implications.[16] Control status is more sensitive to clinical changes than risk level, phenotype, or Global Strategy

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for Objective Lung Disease (GOLD) classification A-D,[17] and loss of control is associated with an increased risk of exacerbation over the following six months.[18] For this reason, clinical control of COPD could be used, particularly in primary care, to assist the physician in deciding to escalate or deescalate treatment to achieve the best clinical outcomes.

The new GesEPOC update must incorporate the evidence that has emerged in recent years on the treatment and follow-up of COPD. It is a great challenge to decide when and how to include changes in a guideline; we must avoid being influenced by trends that can be short-lived and not always well founded, but remain flexible enough to incorporate advances that help professionals and patients manage this still highly prevalent disease.[19]

Statement of interest

MM has received honoraria for speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Menarini, Rovi, Bial, Sandoz, Zambon, CSL Behring, Grifols and Novartis, consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Bial, Gebro Pharma, Kamada, CSL Behring, Laboratorios Esteve, Ferrer, Mereo Biopharma, Verona Pharma, TEVA, Spin Therapeutics, pH Pharma, Novartis, Sanofi and Grifols and research grants from GlaxoSmithKline and Grifols.

MC has received honoraria for speaking engagements from AstraZeneca, Bial, Boehringer Ingelheim, Chiesi, Gebro Pharma, GlaxoSmithKline, Menarini, Novartis, CSL Behring and Grifols and consulting fees from Chiesi and GlaxoSmithKline.

JJSC has received honoraria for speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Esteve, Ferrer, GSK, Menarini, Novartis, and Pfizer, and consulting fees from AirLiquide, Boehringer Ingelheim, Chiesi, GSK, AstraZeneca, Ferrer and Novartis.

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