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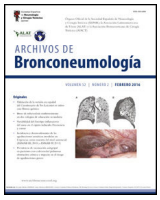

Scientific Letter

[Translated article] Initial Treatment in Chronic Obstructive Pulmonary Disease According to GesEPOC 2021 vs. GesEPOC 2017. Approaching Criteria With GOLD 2021?

Tratamiento de inicio en la enfermedad pulmonar obstructiva crónica, según GesEPOC 2021 vs. GesEPOC 2017, ¿acercando criterios con GOLD 2021?

To the Director,

In Spain, the Global Initiative for Chronic Obstructive Lung Disease (GOLD)[1] and the Spanish Chronic Obstructive Pulmonary Disease Guidelines (GesEPOC)[2] are the main publications on which recommendations for the diagnosis and treatment of chronic obstructive pulmonary disease (COPD) are based. The newly released GesEPOC 2021 has modified the previous version[3] in several ways, and we would like to highlight two changes in particular: (1) the lowering of the threshold for high-risk dyspnea, and (2) the recommended use of the long-acting beta2-agonist/inhaled corticosteroid (LABA/ICS) combination as the preferred initial treatment in patients with eosinophilic inflammation and a history of exacerbations. In contrast, the previous version recommended this treatment for all high-risk subjects with asthma-COPD overlap (ACO) phenotype, regardless of their history of exacerbations. Consequently, the application of the new GesEPOC guidelines will foreseeably involve changes with respect to the previous indication of pharmacological treatment in a certain proportion of subjects, but this hypothesis has not yet been explored. Moreover, the new guidelines co-exist with GOLD 2021 which, unlike GesEPOC, classifies and recommends treatment according to symptoms and history of exacerbations, without taking into account lung function. This could lead to significant discrepancies in the choice of initial treatment of COPD patients, depending on the therapeutic algorithm adopted by the physician.[4]

The aim of this study was to analyze the magnitude and characteristics of any changes in the initial treatment of COPD patients required by the application of GesEPOC 2021 compared to the 2017 version, and to evaluate the degree of concordance of both versions with GOLD 2021. To this end, we conducted a simulation study from a database of real patients diagnosed with COPD who were followed up in a respiratory medicine clinic. We included subjects for whom the following variables were recorded at their first visit to the clinic: forced expiratory volume in 1 second (FEV_1)% postbronchodilator; classification of the patient as an exacerbator (≥ 2 exacerbations treated with steroids and/or antibiotics or an exacerbation requiring hospital admission in the year prior to the first visit) or non-exacerbator (did not meet any of the previous premises); baseline dyspnea according to the Modified Medical Research Council (mMRC) score; and peripheral blood eosinophil count in the year prior to the first visit. Patients were classified according to GesEPOC 2021 as high or low risk. Patients at high risk were classified as "non-exacerbators", "non-eosinophilic exacerbators", or "eosinophilic exacerbators" according to the presence of exacerbations and their eosinophil count in blood.[2] In the case of the GesEPOC 2017 classification, the risk criteria applied were similar to version 2021 except for the degree of dyspnea, where mMRC 0–2 was considered low risk. The criteria indicated by GesEPOC 2017[3] were used for the diagnosis of ACO. For the purposes of this study, we worked from the premise that patients would not have previously received bronchodilator treatment, and as such, were considered naïve.

In order to simplify the analysis, and given the difficulty of deciding among bronchodilators with different mechanisms of action in a study of these characteristics, we limited the choice of pharmacological treatments to three possibilities, according to the algorithms recommended by each guideline: (1) use of a single bronchodilator (1 BD); (2) use of dual bronchodilation (2 BDs); and (3) indication of LABA/ICS. In both versions of GesEPOC, 1 BD was indicated for low-risk patients and 2 BDs for high-risk patients, with the exception of those who met criteria for ACO (GesEPOC 2017) or eosinophilic exacerbator (GesEPOC 2021), in whom LABA/ICS would be indicated.[2,3] With respect to GOLD 2021, patients in groups A, B and C were prescribed treatment with 1 BD. One BD was indicated in group D, except in the most symptomatic cases who presented dyspnea mMRC > 2, whose recommended treatment was 2 BDs; subjects with peripheral blood eosinophil ≥ 300 cells/L were prescribed LABA/ICS.[1] A descriptive analysis was performed, and concordance between the different treatments was analyzed with the overall unweighted Kappa index. The analysis was approved by the Ethics Committee of Hospital Universitario Nuestra Señora de Candelaria.

In total, 335 patients were selected for whom all information was available for analysis. Age (median [interquartile range]) was 70 [62–77]) years; 271 (80.9%) were men; FEV_1% was 53 (42–68); and pack-year index 41.5 (35–60). A total of 112 (33.4%) had ≥300 eosinophils/L in their blood count.

Table 1 shows the relationship between the ABCD classification of GOLD and the high/low risk classification of both versions of GesEPOC and their initial treatments. In contrast to GesEPOC 2017, the GesEPOC 2021 classification (with the new dyspnea threshold) results in the low-risk group being exclusively made up of subjects in the GOLD 2021 group A, while patients in GOLD 2021

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Table 1
Classification of patients and treatment allocation according to GOLD and GesEPOC.

	GOLD 2021 ABCD (number of patients)			
A. Correlation between groups classified according to GOLD 2021 and GesEPOC				
GesEPOC 2021 (number of patients)	A (119)	B (137)	C (15)	D (64)
Low risk (90)	90	0	0	0
High risk (245)	29	137	15	64
GesEPOC 2017 (number of patients)				
Low risk (155)	92	63	0	0
High risk (180)	27	74	15	64
Treatment	GOLD *n* (%)	GesEPOC 2021 *n* (%)	GesEPOC 2017 *n* (%)	
1 BD	298 (89%)	90 (26.9%)	155 (46.3%)	
2 BDs	13 (3.9%)	214 (63.9%)	128 (38.2%)	
LABA/ICS	24 (7.2%)	31 (9.3%)	52 (15.5%)	

1 BD: 1 bronchodilator; 2 BDs: dual bronchodilation; LABA/ICS: beta2-agonist/inhaled corticosteroid; GOLD: Global Initiative for Chronic Obstructive Lung Disease; GesEPOC: Spanish Chronic Obstructive Pulmonary Disease Guidelines.

group B are all included in the high-risk group. From a therapeutic point of view, GesEPOC 2021 involves a marked increase in dual bronchodilatation compared to single bronchodilatation (which can be justified by a higher proportion of patients labeled as high risk), and a decrease in the initial use of LABA/ICS. The new GesEPOC 2021 guidelines, by not including the ACO phenotype in the initial treatment algorithm and focusing on the use of ICS in high-risk subjects with eosinophilic exacerbator phenotype, result in an indication of LABA/ICS that is similar to the GOLD 2021 recommendations. The application of the GOLD algorithm, in the conditions we established, results in less intense treatment than both versions of GesEPOC. GesEPOC promotes a greater use of dual bronchodilatation, possibly due to the inclusion of FEV_1 in its therapeutic algorithm. The degree of concordance between the 2 versions of GesEPOC was higher (Kappa index: 0.53, 95% confidence interval [CI] 0.46–0.60) than between GOLD 2021 and GesEPOC 2021 (Kappa: 0.14, 0.09–0.19) or between GOLD 2021 and GesEPOC 2017 (Kappa: 0.22, 0.15–0.28).

Our study has some obvious limitations: the therapeutic schedules we applied are a simplified version of all possible pharmacological treatments, and the study was conducted in a specialized care setting that is not representative of all levels of care. Overall discrepancies between different treatments could have been less pronounced if a greater number of less severe patients had been included. The CAT questionnaire was not used, so the distribution of GOLD groups in both GesEPOC guidelines could vary. Due to the study design, some possible alternative treatments accepted by GesEPOC 2021 have not been included. Only initial treatments were analyzed, as set out in the study plan, and it is plausible that subsequent modifications to this original therapeutic scheme could reduce long-term variability between the various documents analyzed.

Nevertheless, this is the first study to evaluate the potential effect of the new GesEPOC guidelines on therapeutic patterns in COPD, which we believe may be considerable. Consequently, we believe that these results are of interest, since the potential impact on clinical outcomes of starting treatment in line with one guideline or another may be relevant, although this is entirely speculative to date.

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Conflict of interests

The authors declare conflicts of interest in the manuscript: Juan Marco Figueira Gonçalves has received honoraria for speaking engagements and funding for conference attendance from Laboratories Esteve, MundiPharma, AstraZeneca, Boehringer Ingelheim, Ferrer, Menarini, Rovi, GlaxoSmithKline, Chiesi, Novartis, and Gebro Pharma. Rafael Golpe has received honoraria for speaking engagements and funding for conference attendance from Laboratorio Esteve, Mundipharma, AstraZeneca, Boehringer Ingelheim, Ferrer, Menarini, Rovi, GlaxoSmithKline, Chiesi, Novartis, and Gebro Pharma. Cristóbal Esteban has received speaker fees and research grants from GlaxoSmithKline, Menarini, and AstraZeneca. Carlos Amado Diago has received honoraria for speaking engagements and/or scientific consultancy from Boehringer Ingelheim, Pfizer, AstraZeneca, Novartis, Chiesi, Faes Farma, Esteve, and GlaxoSmithKline. Ignacio García Talavera has honoraria from GSK, AstraZeneca, Pfizer, Chiesi, and Grifols for speaking engagements, studies and/or scientific consultancy. Carolina Ramos Izquierdo declares no conflict of interest.

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