

Usefulness of the Guidelines of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) in Identifying the Causes of Chronic Cough

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OBJECTIVE: The usefulness of the recently published guidelines of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) on the diagnosis and treatment of chronic cough has not yet been demonstrated. The objectives of the present study were *a*) to evaluate the usefulness of the SEPAR guidelines for identifying the possible causes of chronic cough, and *b*) to determine the most frequent causes of chronic cough treated by primary care physicians.

METHODS: We carried out a prospective descriptive study that included 57 consecutive patients (mean age, 62 years) seeking medical attention for chronic cough in a primary health care area. The patients were evaluated using the algorithm proposed in the SEPAR guidelines, whereby the diagnostic procedure is divided into 3 phases in function of complexity. Phase I was carried out at the primary care level, and phases II and III at a hospital pneumology department.

RESULTS: For 56 patients (98%), the potential cause of cough was identified for 52 (91%) in phase I; for 3 (5%), in phase II; and for 1 (2%), in phase III. In 30 patients (53%), a single cause was identified; in 20 (36%), 2 causes; and in 6 (11%), more than 2 causes. Considered individually, the most common causes were postnasal drip in 26 cases (46%), the use of cough-inducing drugs (10 of them attributable to angiotensin-converting enzyme inhibitors) in 16 (28%), asthma in 15 (27%), infection in 13 (23%), gastroesophageal reflux in 12 (21%), and others in 9 (16%).

CONCLUSIONS: The application of the SEPAR guidelines on chronic cough is useful for the identification of its causes. The use of angiotensin-converting enzyme inhibitors is a frequent cause of coughs diagnosed at the level of primary outpatient health care.

Key words: *Chronic cough. Chronic cough, causes. Chronic cough, diagnosis. SEPAR guidelines.*

Eficacia de la normativa SEPAR en la identificación de las causas de tos crónica

OBJETIVO: Recientemente, la Sociedad Española de Neumología y Cirugía Torácica (SEPAR) ha editado una normativa para el diagnóstico y tratamiento de la tos crónica, cuya eficacia aún no se ha demostrado. Los objetivos del presente estudio han sido: *a*) evaluar la eficacia de la normativa SEPAR en la identificación de las posibles causas de tos crónica, y *b*) determinar las causas de tos crónica más frecuentes en el nivel de la atención primaria sanitaria.

MÉTODOS: Se ha realizado un estudio descriptivo y prospectivo que incluyó consecutivamente a 57 pacientes (media de edad de 62 años) que consultaron por tos crónica en un área básica de salud. Se les evaluó según el algoritmo propuesto en la normativa SEPAR, que distribuye en 3 fases el proceso diagnóstico a seguir dependiendo de su complejidad. La primera de éstas, la fase I, se realizó en el nivel asistencial de la atención primaria, y las fases II y III, en la consulta de neumología hospitalaria.

RESULTADOS: En 56 pacientes (98%) se consiguió identificar la causa potencial de la tos, en 52 (91%) en la fase I, en 3 (5%) en la fase II y en uno (2%) en la fase III. En 30 pacientes (53%) se constató una sola causa de tos, en 20 (36%) se evidenciaron 2 y en 6 (11%), más de 2. Consideradas individualmente, las causas más frecuentes observadas fueron: en 26 casos (46%), goteo nasal posterior; en 16 (28%), ingesta de fármacos desencadenantes de tos (10 de ellos inhibidores de la enzima de conversión de la angiotensina); en 15 (27%), asma; en 13 (23%), infecciosa; en 12 (21%), reflujo gastroesofágico, y en 9 (16%), otras.

CONCLUSIONES: La aplicación de la normativa SEPAR sobre la tos crónica es eficaz en la identificación de sus causas. La tos por la toma de inhibidores de la enzima de conversión de la angiotensina es una causa frecuente en el nivel extrahospitalario básico sanitario.

Palabras clave: *Tos crónica. Causas de tos crónica. Diagnóstico de tos crónica. Recomendaciones SEPAR.*

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Introduction

A cough that persists for more than 3 weeks and is unrelated to an acute process is termed chronic.¹ In Spain chronic cough accounts for between 10% and 20% of all outpatient consultations of a pneumologist.²

After asthma and chronic obstructive pulmonary disease (COPD), it constitutes the third cause of referral from primary care to a lung specialist.³

Several studies have shown that a systematic approach to the etiologic diagnosis of cough by applying protocols and decision algorithms has a high diagnostic yield (92%-96%).^{4,5} The Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) recently published guidelines on appropriate diagnostic and therapeutic management of chronic cough.⁶ In these guidelines a sequential decision algorithm to identify the causes of cough was proposed, and 3 stages of diagnostic activity were established in accordance with the frequency of causes of cough, the rational use of diagnostic resources, and the complexity of the tests to be performed. In view of the recentness of these guidelines, no studies have yet determined the applicability of the algorithm and, consequently, the usefulness of the guidelines.

In addition, the true frequencies of causes of chronic cough are unknown. Most of the studies available have been carried out in outpatient pneumology clinics or in hospital pneumology departments,^{5,7} and the patients included in these series had therefore already been referred from primary care centers. The frequencies of causes of cough observed were not, therefore, representative of the general population. Thus, 1 study

found that in up to 13% of the population sample analyzed, cough was produced by so infrequent a disease as eosinophilic bronchitis.⁸

We designed the present study with the 2 objectives of evaluating the efficacy of the diagnostic algorithm proposed in the SEPAR guidelines for the identification of the causes of chronic cough⁶ and of determining the frequencies of these causes at the first level of primary health care.

Methods

We carried out a prospective descriptive study designed to evaluate the usefulness of the SEPAR guidelines⁶ in identifying the possible causes of chronic cough. We included in our study patients over 14 years old, of both sexes, with chronic cough of unknown etiology. They were patients of 13 primary care physicians assigned a total caseload of 22 894 inhabitants, in the "Congrès" Basic Health Care Area within one of the reorganized primary public health care delivery centers in Barcelona, Spain, a clinic facility which also has a specialized pneumology department. We considered cough to be chronic if, in addition to being the reason for consultation, it was the patient's main symptom, had lasted more than 3 weeks, and the underlying cause was unknown. Those patients who met the inclusion criteria were enrolled consecutively over the 3-month period between November

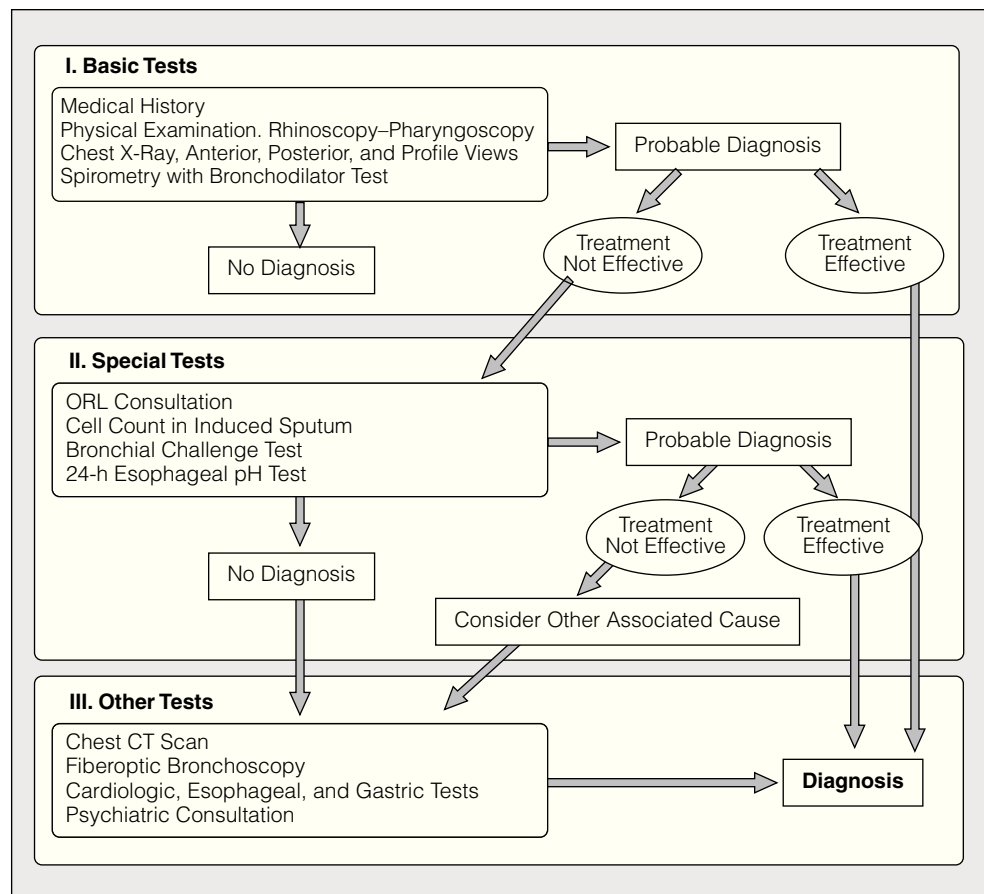


Figure. Sequential algorithm proposed in the SEPAR guidelines⁶ to identify causes of chronic cough. SEPAR indicates Spanish Society of Pulmonology and Thoracic Surgery; ORL, otorhinolaryngology; CT, computed tomography.

2001 and February 2002. Patients who had been active smokers for at least a year before the beginning of the study and those receiving corticosteroid or immunodepressant treatment were excluded.

All the patients in the study came from the caseloads of the 13 participating primary care physicians and, after undergoing spirometry and radiography, were assessed in a second consultation by 1 of the 2 authors of this study (LR or MPL), who are primary health care physicians at the aforementioned facility. The tests recommended in stage I of the guidelines⁶ were carried out at the center. Stage I included a structured medical history to identify the possible causes of cough, a physical examination together with simple pharyngoscopy, and the tests shown in the Figure (taken from the SEPAR guidelines). Spirometry, including a bronchodilator test, was performed by personnel from the pneumology department of the hospital in the same primary health care area following SEPAR recommendations.⁹ If conclusions based on the medical history or the results of any of the complementary tests pointed to a possible cause, treatment was initiated according to the therapeutic recommendations formulated in the guidelines on chronic cough. A conclusive diagnosis was established when cough disappeared or was substantially reduced as a result of treatment. When the information did not lead to suspicion of a possible cause, or when the treatment of a possible cause did not lead to a favorable clinical response, the patient was referred to the pneumology department of the Santa Creu i Sant Pau Hospital in Barcelona, Spain for stages II and III of the diagnostic algorithm for chronic cough. Despite therapeutic failure, the patient was encouraged not to abandon the prescribed treatment.

Another overall evaluation was carried out in the hospital, with another medical history taken and the appropriate tests ordered as recommended in stages II and III (shown in the Figure). The usual techniques for each test were used in each case.¹⁰⁻¹² As in stage I, if the results of the tests pointed to a

possible diagnosis, treatment was initiated. In the absence of a diagnosis or a favorable response to treatment, the patient underwent the tests reserved for stage III of the algorithm.

Statistical analysis included a description of the population sample evaluated and of the variables used, the total percentage for all the causes of cough identified, and the individual frequency of each cause.

Results

A total of 57 patients (approximately 65% women) with chronic cough, mean age 62 years (range, 16-88 years), were enrolled in the study. Forty-seven percent of the patients had a cough lasting more than 6 months (range, 1-620 months). The number of tests performed is shown in Table 1. In accordance with the SEPAR guidelines,⁶ an average of 3 tests were performed per patient in stage I, 4.4 in stage II, and 2 in stage III (Table 1). For the population sample as a whole, applying the algorithm meant a mean of 3.5 tests per patient. The main characteristics of the cough, associated symptoms, and stage I test results are shown in Table 2.

An etiologic diagnosis was determined in stage I of the SEPAR algorithm for 52 patients (91%); in stage II, for 3 (5%); and in stage III, for 1 (2%). For 1 patient (2%), no conclusive cause was identified. A single cause was identified for 30 patients (53%); 2 causes for 20 (36%); and more than 2 causes for 6 (11%). The possible causes of cough identified individually, independent of the fact that several of them can occur together in a given patient, were postnatal drip in 26 patients (46%), the use of cough-inducing drugs (10

TABLE 1
Total Number of Complementary Physical Examinations Performed at Each Stage (of the SEPAR Guidelines on Chronic Cough⁶) in Order of Frequency*

	Number	Tests or Visits per Patient, Mean
Stage I (n=57)		
Spirometry with bronchodilator test	62	
Chest x-ray	57	
X-ray of paranasal sinuses	57	
Total	176	3.1
Stage II (n=5)		
Methacholine challenge test	5	
Induced sputum inflammatory cell count	5	
Otorhinolaryngological examination	4	
Detection of anti-Ro and anti-La antibodies in plasma	3	
Head CT scan of paranasal sinuses	2	
Skin prick allergy tests	2	
24-hour esophageal pH test	1	
Total	22	4.4
Stage III (n=2)		
Chest CT scan	1	
Fiberoptic bronchoscopy	1	
Echocardiography	1	
Psychiatric consultation	1	
Total	4	2
All stages	202	3.5

*SEPAR indicates Spanish Society of Pulmonology and Thoracic Surgery; CT, computed tomography.

cases attributable to angiotensin-converting enzyme inhibitors, 4 to β -blockers, 1 to angiotensin II receptor antagonists, 1 to a diuretic, and 1 to another antihypertensive drug) in 16 (28%), asthma in 15 (27%), cough subsequent to respiratory infection in 13 (23%), gastroesophageal reflux in 12 (21%), and other causes (chronic bronchitis or COPD in 4 patients, exposure to toxins in the work place in 2, bronchiectasis in 4, chronic pharyngolaryngitis in 1, and eosinophilic bronchitis in 1) in 9 patients (16%). The most frequently observed combinations of possible causes were the use of cough-inducing drugs together with postnatal drip in 4 patients (7%); and postnasal drip together with asthma in 2 (3.5%). There were other possible coexisting causes in 23 of the 16 patients who were taking cough-inducing drugs, and some other cause was suspected in 10 of the 12 patients with gastroesophageal reflux. The potential causes of cough in the 3 patients diagnosed in stage II were postnasal drip and asthma in 1 patient, postnasal drip, asthma, and gastroesophageal reflux in another, and use of cough-inducing drugs and gastroesophageal reflux in the third. Ultimately, the cause of cough was bronchiectasis in the patient diagnosed in stage III. Finally, the patient for whom no definite cause of cough was identified despite the tests performed (including stage III tests) had a high percentage of eosinophils in induced sputum (approximately 15%; reference cutoff, 3%), and this led to a diagnosis of possible eosinophilic bronchitis as the cause of cough. However, treatment with inhaled corticosteroids did not improve the patient's symptoms.

Discussion

The main conclusion of our study was that the SEPAR guidelines⁶ are indeed useful in identifying the possible causes of chronic cough or diseases that can trigger it. Some studies have shown that the clinical data usually collected for cough (such as type, frequency, intensity, whether or not it is seasonal, presence of expectoration, whether or not is triggered by swallowing) do not allow certain or tentative identification of its cause.^{13,14} For this reason, it is indispensable to perform complementary tests to determine these causes. In order to rationalize the indication of such tests, the use of sequential algorithms that take into consideration the different prevalences of the possible causes of chronic cough has been recommended. Noteworthy among these algorithms are those based on a protocol in which the anatomical sites involved in the cough reflex are studied. The most often cited of these algorithms are those of Irwin et al.^{4,15} and Poe et al.¹⁶ Several studies have confirmed the efficacy of these and other similar sequential algorithms, showing their diagnostic yield to be greater than 90%.^{4,7} A recent study carried out in Spain evaluating the efficacy of the algorithm of Irwin and colleagues in 110 patients showed that the cause of cough could be identified in 97% of cases when the process was

TABLE 2
Main Characteristics of Cough, Associated Symptoms, and Tests Performed at Stage I (of the SEPAR Guidelines on Chronic Cough⁶) in the 57 Patients*

Characteristics of cough	
Nighttime	34
Daytime	66
Productive	42
Nonproductive	58
Symptoms associated with cough	
Nasal obstruction and/or rhinorrhea and/or sneezing	47
Dyspnea and/or wheezing	25
Heartburn and/or food reflux	23
Chronic expectoration	12
Bloody sputum	4
Fever	4
Chest pain	2
Tests	
Abnormal paranasal sinus x-ray	25
Chest x-ray suggestive of lung field pathology	2
Spirometry	
FEV ₁ (<80% of predicted)	33
Significant BDT (>12% or \geq 200 mL baseline FEV ₁)	32

*Values are percentages of the total population sample analyzed. SEPAR indicates Spanish Society of Pulmonology and Thoracic Surgery; FEV₁, forced expiratory volume in 1 second; BDT, bronchodilator test (following salbutamol inhalation).

applied.⁵ Consistent with the results of previous series applying the algorithm proposed in the SEPAR guidelines⁶ allowed us to identify the possible causes of chronic cough in 98% of the patients evaluated.

What the SEPAR algorithm adds to the above-mentioned anatomic approach on which it is based is the recognition of new diseases that may cause cough, such as eosinophilic bronchitis,^{17,18} and the incorporation into the algorithm of noninvasive examinations, such as inflammatory cell count in induced sputum, thus broadening the diagnostic range.^{19,20} The test complements proposed by the guidelines are in line with the recent recommendations of international experts published subsequently.²¹ In addition, the guidelines divide this testing into 3 stages, according to complexity and availability: stage I, or the basic study, should always be considered during an initial evaluation and, therefore, be carried out at primary health care centers; stages II and III should be reserved for pneumology departments in a hospital environment. One of the results of our study that should be highlighted here is that in as many as 91% of patients the cause of cough was identified as early as stage I, that is, at the primary care level. This demonstrates that it is indeed feasible to carry out stage I at the primary care level, and that the proper application of the algorithm enhances the problem-solving ability of primary care physicians in diagnosing chronic cough and helps them make the decision to refer patients to specialists, thereby increasing the usefulness of the guidelines.

Nonetheless, this ability to solve problems requires that primary health care physicians have rapid access to the various complementary diagnostic tests of stage I, particularly to spirometry. It must be remembered that

in our study, due to the particular logistic arrangement that results from the way the relation between primary care and specialized hospital care is organized in our health care area,²² spirometry is performed and interpreted at the primary health care center by professionals from the hospital pneumology setting. This is in clear contrast to the general situation of primary health care in Spain where, with some exceptions, spirometry is not yet sufficiently widespread^{23,24} or is performed with unacceptable technical shortcomings that considerably limit its real usefulness.

Another aspect of the present study that is worthy of attention is the relatively low number of complementary tests needed to reach the final etiologic diagnosis of chronic cough (a mean of 3.5 per patient). In view of the possible increase in consumption of health care resources (repeated visits to physicians, tests, and the prescription of inappropriate treatment) that a delay in identifying the cause of cough may lead to, the reduced need for complementary tests resulting from the application of the SEPAR guidelines⁶ means a more rational use of health care resources and contributes to greater efficiency in the process of diagnosing cough.

The frequencies of the various causes of chronic cough have been evaluated in many studies.^{1,4,5,7,16} While a comparison of the results does show certain differences, once COPD and smoking have been eliminated, the most frequently mentioned causes are usually postnasal drip (8%-87%), asthma (20%-33%), and gastroesophageal reflux (10%-21%). In our study as well, postnasal drip (46%), asthma (27%), and gastroesophageal reflux (21%) were among the 4 most frequent causes. The finding that in as many as 23% of patients cough was caused by a respiratory infection can be explained by the fact that data were collected in winter and that we considered cough to be chronic if it lasted 3 weeks. Other authors have established longer time periods of up to 8 weeks.^{25,26}

One of the most interesting findings of the present study was the high frequency at the primary care level of drug-induced cough (28%), particularly due to the use of angiotensin-converting enzyme inhibitors (18%). This circumstance has not been sufficiently evaluated in other series because patients using such drugs have been excluded from the studies, and the real frequency, therefore, remains unknown. Another interesting finding is the low proportion of eosinophilic bronchitis as a cause of cough—it was identified in only 1 patient whose cough continued after treatment. We also found the presence of more than 1 cause of cough in a single patient to be frequent (47%), as has been observed in other studies (18%-62%).^{1,4,5,7,16}

The rational use of diagnostic resources grouped in the 3 stages recommended by the SEPAR guidelines on chronic cough⁶ is effective in identifying the causes of chronic cough and may increase the efficiency of available health care resources.

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