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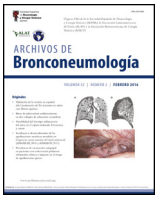

Original Article

Utility of Induced Sputum in Routine Clinical Practice☆

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ABSTRACT

Objective: To determine the general and specific utility in diagnosis and/or treatment of induced sputum (IS) inflammatory cell counts in routine clinical practice.
Methods: Retrospective study of 171 patients referred for clinical sputum induction over a 1-year period in the pulmonology department of a referral hospital. Independent observers established whether the information provided by IS inflammatory cell count was useful for making diagnostic and therapeutic decisions.
Results: The most frequent reasons for determination of IS inflammatory cell count were: asthma 103 (59.20%); uncontrolled asthma 34 (19.54%); chronic cough 19 (10.9%), and gastroesophageal reflux 15 (8.6%). In 115 patients (67.3%) it was generally useful for diagnosis and/or treatment; in 98 patients (57.3%) it provided diagnostic information and in 85 patients (49.7%) it assisted in therapeutic decision-making. In asthma, uncontrolled asthma, chronic cough and gastroesophageal reflux, the results were useful in 71.8%, 67.6%, 47.4% and 60%, respectively.
Conclusion: The information provided by IS inflammatory cell count is extremely useful in clinical practice, especially in asthma and chronic cough. These results may justify the inclusion of the IS technique in pulmonology departments and asthma units of referral centers.

Utilidad del esputo inducido en la práctica clínica habitual

Palabras clave:
Asma
Esputo inducido
Utilidad clínica

RESUMEN

Objetivos: Determinar la utilidad general y específica (diagnóstica y/o terapéutica) del recuento de las células inflamatorias (RCI) del esputo inducido (EI) en situación de asistencia clínica real.
Métodos: Estudio retrospectivo que incluyó a los 171 pacientes que durante un año se les recogió un EI para determinar su RCI en un servicio de Neumología de un hospital de referencia. Observadores independientes al equipo médico habitual establecieron si la información proporcionada por el RCI del EI fue útil en la toma de decisiones diagnósticas y terapéuticas.
Resultados: Las causas más frecuentes que motivaron la solicitud del RCI del EI fueron: asma 103 (59,20%); asma de control difícil 34 (19,54%); tos crónica 19 (10,9%), y reflujo gastroesofágico 15 (8,6%). En 115 (67,3%) pacientes el RCI del EI resultó clínicamente útil (valoración general); en 98 (57,3%) proporcionó información diagnóstica, y en 85 (49,7%), información terapéutica relevante. En el asma, asma de control difícil, tos crónica y reflujo gastroesofágico fue útil en el 71,8, el 67,6, el 47,4 y el 60%, respectivamente.
Conclusiones: La información proporcionada por el RCI del EI resulta de gran utilidad en la práctica clínica, particularmente en el asma y la tos crónica. Estos resultados podrían proporcionar argumentos para recomendar la incorporación de la técnica en los servicios de Neumología de referencia y en las unidades de excelencia de asma.

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Introduction

Bronchial inflammation plays a major role in the pathogenesis of important respiratory tract diseases, such as asthma or chronic obstructive lung disease (COPD). A tool for evaluating the type and intensity of bronchial inflammation would be of great benefit in the assessment and control of these diseases, particularly in the more severe forms.

Endobronchial biopsy is the gold standard in the study of bronchial inflammation; being an invasive procedure, however, its use as a diagnostic tool is limited.[1] Accordingly, interest is growing in non-invasive procedures, and new techniques for measuring fractional exhaled nitric oxide (FE_{NO}) and inflammatory cell count (ICC) in induced sputum (IS) are attracting particular attention.

While FE_{NO} identifies eosinophilic bronchial inflammation, it does not recognize other inflammatory types, so its utility is limited.[2] IS is a validated standardized technique, considered the gold standard non-invasive methods for evaluating bronchial inflammation and for distinguishing between inflammatory phenotypes.[3] Its clinical applications are becoming more refined, and it is of particular benefit in asthma, due to its high yield. It can be used as a complementary diagnostic tool in asthma,[4] and is of benefit in determining inflammatory phenotypes,[5] adjusting treatment, and predicting therapeutic response.[6,7] It has also been indicated in the management of difficult-to-control asthma (DCA) in Spanish and international guidelines.[8–10] Its use is not restricted purely to asthma: it is also useful for determining the etiology of chronic cough,[11,12] gastroesophageal reflux (GER)[13] and other entities, such as COPD, infectious diseases, eosinophilic bronchitis, lung cancer, interstitial lung diseases, and heart failure.[14–19]

However, despite its validity and applicability, ICC in IS is not routinely performed in standard clinical practice, probably because it requires a certain degree of technical experience in obtaining, manipulating and interpreting the samples, in addition to being laborious and costly. Nevertheless, the data provided by IS testing is so obviously of interest[10] that we are surprised how rarely it is used in high-level pulmonology departments. The aim of this study was to evaluate the contribution of ICC in IS in healthcare practices.

Methods

Design

This was a retrospective, descriptive study performed in standard clinical practice to determine the clinical utility of ICC in IS.

Study Population

All patients who underwent ICC in IS as part of their standard care in the pulmonology department of our hospital over the course of 1 year (May 2012–May 2013) were included, irrespective of their previous treatment, which often included inhaled corticosteroids (ICS), particularly in asthma patients. Patients who underwent the procedure for exclusively investigational purposes were excluded.

Ethical and Legal Aspects

Since this was a descriptive, retrospective study performed in standard clinical practice conditions, the Clinical Research Ethics Committee was informed only of our interest in collecting this information from the clinical records of the patients. All study data collection was anonymous.

Primary Endpoints

The primary endpoint was the proportion of patients in whom IS was clinically useful. IS was considered useful when the ICC provided information that could be used for establishing a diagnosis and/or when it led directly to a decision on therapeutic management. Three observers, independent from the treating physicians (SB, LS, and GC), assessed these premises by reviewing the clinical records.

The asthma group included patients with clinically suspected asthma and those with a previous diagnosis of asthma. In the DCA group, all patients had asthma meeting criteria for poor control. IS was considered of use in diagnosis when the determination of bronchial eosinophilia led to the diagnosis of patients with a clinical history consistent with asthma.[20] It was also classified as useful in patients with a previously established diagnosis of asthma or DCA, when the determination of the inflammatory phenotype helped clarify the nature of the patient's respiratory symptoms[9,10,21] in the following circumstances: suspicion of poor treatment compliance, exposure to airborne allergens, or insufficient treatment in the case of an eosinophilic phenotype; suspicion of an erroneous diagnosis or another associated disease or resistance to corticosteroids in the case of bronchial neutrophilia; a paucigranulocytic phenotype suggested controlled eosinophilia, confounding diagnoses, or paucigranulocytic variables. IS was considered therapeutically useful in the following situations: in patients with bronchial eosinophilia when the decision was taken to increase ICS, initiate systemic corticosteroids (SCS), initiate interventions for improving compliance, or initiate leukotriene receptor antagonists;[6,7] in patients with a neutrophilic phenotype[6,7] when antibiotics or long-acting β2-agonists were initiated or ICS dosing was reduced; and in patients with a paucigranulocytic phenotype when the addition of long-acting β2-agonists was evaluated or the steroid dose was reduced.[6,7]

In patients with chronic cough, ICC was considered to be useful when findings helped identify the reason for the cough[11,12] in the following circumstances: a case of bronchial eosinophilia arousing suspicion of asthma, eosinophilic bronchitis, or occupational disease; or a neutrophilic phenotype aroused suspicion of infectious bronchitis or bronchiectasis. IS was considered of therapeutic utility when findings led to the initiation of ICS or antibiotic therapy. Finally, the finding of lipophages in patients with chronic cough or clinically suspected GER helped identify a diagnosis of GER. Initiation of antacids or antireflux measures was considered a therapeutic contribution.

Secondary Endpoints

Demographic, clinical and functional data were collected from all patients, and the main reasons for requesting IS and the characteristics of the sample (cell count, sample quality and inflammatory phenotype) were recorded.

Procedures

Spirometry

Spirometry was performed using a Daptospir-600 device (Sibelmed SA, Barcelona, Spain), by an experienced operator, following SEPAR 2013 guidelines.[22] The reference values were those established for a Mediterranean population.[23]

Fractional Exhaled Nitric Oxide

This was carried out using an electrochemical device (NO Vario Analyzer. FILT Lungen and Thorax Diagnostic GmHb, Berlin, Germany) at a flow of 50 ml/s, following the recommendations of