Respiratory Medicine 124 (2017) 21–29

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

The level of diagnostic assessment in severe asthma: A nationwide real-life study

Anna von Bülow [a, *], Vibeke Backer [a], Uffe Bodtger [b, c, d], Niels Ulrik Søes-Petersen [d], Karin Dahl Assing [e], Tina Skjold [f], Celeste Porsbjerg [a]

[a] Respiratory Research Unit, Department of Respiratory Medicine, Bispebjerg University Hospital, Bispebjerg Bakke 66, 2400 Copenhagen NV, Denmark
[b] Department of Respiratory and Internal Medicine, Naestved Hospital, Denmark
[c] Institute for Regional Health Research, University of Southern Denmark, Denmark
[d] Department of Respiratory and Internal Medicine, Roskilde Hospital, Denmark
[e] Department of Respiratory Medicine, Aalborg University Hospital, Denmark
[f] Department of Respiratory Medicine, Aarhus University Hospital, Denmark

ARTICLE INFO

Article history:
Received 22 July 2016
Received in revised form
24 January 2017
Accepted 25 January 2017
Available online 27 January 2017

Keywords:
Asthma
Asthma diagnosis
Asthma assessment
Severe asthma
Asthma management
Difficult to treat asthma

ABSTRACT

Introduction: Systematic assessment of patients with severe asthma is pivotal to decide which patients are eligible to new biological therapies. However, the level of diagnostic work-up in patients with severe asthma is only poorly investigated.
Aims & objectives: To describe the diagnostic work-up in a complete population of patients with severe asthma including: objective confirmation of the asthma diagnosis, and identification of potential treatment barriers, such as poor adherence and poor inhaler technique.
Methods: A retrospective cross-sectional multicenter study was performed in 2013. We evaluated patient record forms of all patients (aged 18–65 years) consecutively referred with asthma to one of five respiratory outpatient clinics over two years. Patients were included in the study, if they fulfilled ERS/ATS guidelines for having severe asthma.
Results: Among 1563 patients with asthma, 98 (6.3%) patients fulfilled the criteria for having severe asthma. The diagnosis of asthma was confirmed objectively in 53/98 patients (54.1%). In total, 83.7% underwent at least one diagnostic test for asthma: reversibility test: 63.3%, PEF: 52% and bronchial challenge test: 21.4%. Among patients eligible for a bronchial challenge test ($FEV_1 \geq 70\%$; negative PEF measurement/reversibility test), only 23.1% had such a test performed. Inhalation technique and adherence were assessed in 19.4 and 30.6% of patients, respectively.
Conclusion: Among patients managed for severe asthma in a specialist setting, only half had the asthma diagnosis confirmed objectively, and adherence and inhaler technique were infrequently assessed.

1. Introduction

With the emergence of novel, but expensive biological treatments for severe asthma, a systematic evaluation of patients with severe asthma becomes decisive to identify the eligible patients to these new therapies [1,2].

The prevalence of severe asthma is estimated to 4–8% [3,4]. Despite being a minority, patients with severe asthma possess the largest burden of morbidity with frequent asthma exacerbations, low quality of life and higher risk of experiencing adverse effects from treatment [5,6]. Severe asthma is defined as asthma that requires intensive asthma therapy, and either remains uncontrolled, or becomes uncontrolled if treatment is down-titrated [1].

However, there are many potential competing causes of poor asthma control in patients with severe asthma [7]. Hence, patients receiving high-dose asthma treatment are recommended to undergo a proper systematic assessment in a specialist setting to confirm the diagnosis of asthma and identify and address potential aggravating comorbidities, poor adherence and environmental triggers before as being classified as having severe asthma [1,2,8,9].

A clinical diagnosis of asthma may be based solely on the

* Corresponding author. Respiratory Research Unit, Department of Respiratory Medicine L, Bispebjerg Hospital, Bispebjerg Bakke 66, 2400 Copenhagen NV, Denmark.
E-mail address: annavonbulow@gmail.com (A. von Bülow).

http://dx.doi.org/10.1016/j.rmed.2017.01.010
0954-6111/

Abbreviations

ENT	Ear, nose and throat specialist
FeNO	Fractional exhaled nitric oxide.
HRCT	High resolution computer tomography
ICD-10	International Classification of Diseases –Tenth revision
PEF	Peak expiratory flow
PRF	Patient record form
ICS	Inhaled corticosteroids
SABA	short-acting beta-2-agonist

presence of typical asthma symptoms, such as episodic breathlessness, chest tightness, wheezing or cough. However, a symptom-based diagnosis is associated with a significant risk of over-diagnosis of asthma [10,12] leading to potential over-treatment. Consequently, international guidelines recommend that the diagnosis of asthma should be confirmed in all patients with asthma by demonstrating variable airflow obstruction [9]. Nevertheless, demonstration of variable airflow obstruction may be difficult [9] and time-consuming in patients receiving high doses of ICS [13]. In addition, no validated protocol exits to confirm the diagnosis in patients with severe asthma [1,2]. Nonetheless, repeated failure of demonstrating variable airflow obstruction with reversibility test and bronchial challenge test should call into question whether the asthma diagnosis is correct [2].

Studies describing a complete clinical population of patients with potential severe asthma are lacking. Previous studies in severe asthma have shown that following a systematic assessment, more than 50% were no longer difficult-to-treat [7,14]. Currently, it remains unknown to which extent patients with severe asthma are systematically assessed in order to objectively confirm the asthma diagnosis and identify competing causes of poor asthma control like poor adherence, comorbidities and environmental triggers.

Despite comprehensive assessment to confirming the asthma diagnosis, the diagnosis may be based solely on symptoms in a minority of patients (e.g. due to low lung function excluding bronchial challenge testing). Consequently, it would seem appropriate that patients with non-confirmed asthma were more extensively assessed in order to investigate airway inflammation, comorbidities and rule out potential alternative diagnosis. However, it is unknown whether this is actually the case.

The aim of this study was to describe the diagnostic work-up in a complete real-life population of patients with severe asthma:

1 Evaluate to which extent patients treated by respiratory specialists for severe asthma had the diagnosis of asthma objectively confirmed by demonstration of variable airflow obstruction.
2. Describe the level of assessment of competing causes of poor asthma control, including adherence, inhalation technique, triggers and comorbidities.
3 Investigate whether the assessment of asthma was different in patients with a non-confirmed asthma diagnosis compared to patients with confirmed variable airway obstruction.

2. Methods

2.1. Design

We performed a “real-life”, retrospective, descriptive, non-interventional cohort study. To achieve a high level of external validity, we identified the complete population of all patients consecutively referred to one of five respiratory outpatient clinics in Denmark (Bispebjerg University Hospital, Aarhus University Hospital, Aalborg University Hospital, Naestved Hospital, Roskilde Hospital) over a two years (2009–2010) with a diagnosis of asthma or suspected asthma (referral ICD-10 code: DJ45-DJ459). To allow time for assessment all patients were evaluated two years after referral. Patients were included in the study population if they fulfilled the criteria for having severe asthma according to the ERS/ATS guidelines [1] after two years of assessment (Fig. 1).

The retrospective study-design was purposefully chosen to avoid bias, as the outcome was to evaluate the diagnostic work-up of severe asthma in specialist care.

2.2. Material

Data were obtained from patient record forms (PRF): all patients had an electronical PRF in which all physicians notes were recorded. In addition, patients had a paper PRF containing test results (spirometry, skin prick test, blood samples etc.). Using the electronic PRF, the study population was identified in a stepwise manner (Fig. 1). First, we identified patients having a physician's diagnosis of asthma or suspected asthma. Patients in whom the referral code was incorrect or patients never assessed by a pulmonologist (e.g. failed to appear in the outpatient clinic) were excluded. Subsequently, asthma severity was analyzed according to the level of treatment after two years of assessment in the outpatient clinic. If patients were dismissed from the outpatient clinic before two years, we analyzed the level of asthma severity at the last visit in the outpatient clinic. At this step, patients were excluded if information regarding current asthma treatment was lacking. In addition, patients were excluded if the paper PRF was missing.

2.2.1. Definition of severe asthma

Patients were included in the study population (Fig. 1) if they had a physician's diagnosis of asthma and fulfilled the criteria of having severe asthma by receiving high dose ICS treatment with a second controller (long acting beta-2-agonist, theophylline or leukotriene-antagonist) or oral steroids at the last visit in the outpatient clinic within the two-year period of observation. Furthermore, they should have received high dose ICS ($\geq$1600 μg budesonide or equivalent) for a minimum of twelve months or oral steroids for minimum six months [1].

2.3. Methods

Data on basic characteristics *i.e.* assessment of asthma symptoms, as well as assessment of smoking history, adherence to treatment, inhaler technique, lung function, diagnostic test, examination for comorbidities and asthma phenotyping was examined within the two-year period of observation (date of first physicians visit in the outpatient clinic and the subsequent two years).

2.3.1. Objective confirmation of the asthma diagnosis

A “confirmed asthma” diagnosis was defined as demonstration of variable airflow obstruction by either one of the following:

- Day-to-day Peak expiratory flow (PEF) monitoring,
- Reversibility test (short-acting beta-2-agonist (SABA) or oral steroids)
- Airway hyperresponsiveness (methacholine, mannitol, exercise test, eucapnic voluntary hyperventilation test).