Respiratory Medicine 117 (2016) 166–173

Contents lists available at ScienceDirect

Respiratory Medicine

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

Profile of difficult to treat asthma patients referred for systematic assessment

N. Radhakrishna [a, *], T.R. Tay [a], F. Hore-Lacy [a], R. Hoy [a], E. Dabscheck [a], M. Hew [a, b]

[a] Alfred Hospital, Allergy, Immunology & Respiratory Medicine (AIRMED), Melbourne, Victoria, Australia
[b] Public Health & Preventive Medicine, Monash University, Victoria, Australia

ARTICLE INFO

Article history:
Received 22 March 2016
Received in revised form
3 June 2016
Accepted 8 June 2016
Available online 14 June 2016

Keywords:
Difficult asthma
Severe asthma
Assessment

ABSTRACT

Aim: We determined the proportion of asthma patients under specialist care who remain difficult-to-treat and might benefit from systematic assessment. We additionally report the characteristics and indications for referral in 90 patients who received systematic assessment for difficult asthma.
Methods: We conducted a three-month prospective audit of our hospital's general asthma clinic. We then analyzed consecutive patients over 18 months referred on for systematic assessment of difficult asthma.
Results: Over 3 months, 22/166 patients (13.3%) in the general asthma clinic were considered likely to benefit from systematic assessment of difficult asthma. These patients had higher inhaled steroid requirements (890 ± 604 mg), lower lung function (FEV1: 65 ± 18%), and more often received GINA step 5 treatment (22.7%). However, 7/22 (32%) of suitable patients were not referred for assessment, mainly due to patient factors.
Over 18 months, 90 patients received systematic assessment for difficult asthma, on account of poor symptom control (62%), frequent exacerbations (44%), poor lung function (42%), patient factors (29%), and diagnostic uncertainty (26%). There was a high disease burden with a mean (±SD) asthma control test score and asthma quality of life questionnaire score of 14 ± 5 and 4.26 ± 1.45 respectively. 80% fulfilled criteria for severe asthma. The majority were either atopic (66.7%) or eosinophilic (54.4%); only 15.6% were neither. Patients had a median of three extra-pulmonary comorbidities, of which most were previously unrecognised.
Conclusion: One-in-eight asthma patients already under specialist care were suitable for systematic assessment of difficult asthma, but a third of these were not referred due to patient factors. Diagnostic uncertainty and patient factors were important indications for systematic assessment. Most patients who underwent systematic assessment exhibited severe asthma phenotypes potentially responsive to targeted treatment, but also had multiple comorbidities. Our results highlight the importance of management strategies to address patient factors, severe asthma biology, and concurrent contributory conditions.

1. Introduction

The majority of patients with asthma respond to currently available treatments but some remain difficult to treat despite high-dose inhaled corticosteroids and long-acting beta-agonists [1,2]. A wide variety of issues may contribute to difficult asthma, and many patients require respiratory specialist input [3,4].

The most complex patients may be challenging to evaluate within standard outpatient consultations, even when performed by specialists. Consequently, there has been a move toward systematic assessment of difficult asthma at dedicated difficult asthma centres

Abbreviations: COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnea; GORD, gastroesophageal reflux disease; Anx/Dep, anxiety/depression; DB, dysfunctional breathing; VCD, vocal cord dysfunction; ACT, Asthma Control Test; AQLQ, Asthma Quality of Life Questionnaire.

* Corresponding author. Alfred Hospital, 55 Commercial Rd, Melbourne, Victoria 3004, Australia.
E-mail addresses: N.Radhakrishna@alfred.org.au (N. Radhakrishna), T.Tay@alfred.org.au (T.R. Tay), F.Hore-Lacy@alfred.org.au (F. Hore-Lacy), drryanhoy@gmail.com (R. Hoy), E.Dabscheck@alfred.org.au (E. Dabscheck), m.hew@alfred.org.au (M. Hew).

http://dx.doi.org/10.1016/j.rmed.2016.06.012
0954-6111/

[5]. A systematic approach offers several advantages over unstructured evaluations. First, systematic assessment may refute a diagnosis of asthma even in patients previously seen by specialists [6–8]. Second, it facilitates the detection and management of key comorbidities and patient factors, prior to consideration of expensive targeted therapies [9,10]. Third, systematic assessment has been shown in uncontrolled studies to improve patient outcomes [11].

However, a number of questions remain around systematic assessment of difficult asthma. First of all, published cohorts of difficult asthma patients assessed in a systematic fashion have not reported a denominator population from which patients are drawn [6–8,12]. Understanding the magnitude of the problem has important implications for shaping health care delivery. A study in the Netherlands estimated that 17% of all asthmatics had difficult asthma based on the presence of poor symptom control or frequent exacerbations despite high intensity asthma medication [13]. However this estimate includes patients who may only require a standard consultation at the level of primary or secondary care, and is not indicative of the need for systematic assessment through a dedicated asthma service.

Next, it is unclear which patients should be referred, and criteria for referral to services providing systematic assessment have not been well defined.

Finally, while the characteristics of patients undergoing systematic assessment have been well described in the United Kingdom and Europe, there is less data from many other parts of the world. Due to the inherent heterogeneity of this group of patients, it is possible that our cohort's demographics and characteristics may differ from that previously described elsewhere.

In 2014, we commenced a systematic assessment protocol at our metropolitan university hospital for asthma patients who remained difficult-to-treat even under specialist care. At its inception, we performed an audit of patients seen at the general asthma clinic to identify those who were thought to benefit from systematic assessment. We also prospectively collected data on the difficult asthma cohort undergoing systematic assessment. Our aims were to:

i) Determine the proportion of general asthma patients already under specialist care who remained difficult-to-treat and were thought to benefit from further systematic assessment.
ii) Describe the major indications for systematic assessment, and;
iii) Characterize patients undergoing systematic assessment in our health care setting, to allow comparisons with cohorts from other health systems.

2. Methods

2.1. Proportion of general asthma clinic patients thought to benefit from systematic assessment

Over a three-month period from 1st June 2014 to 31st August 2014, we undertook a cross-sectional audit of the Alfred Hospital general asthma clinic in Melbourne, Australia. This asthma clinic is located at a metropolitan tertiary center, and patients are seen at the request of general practitioners or, on occasion, specialists in the community. For each asthma patient seen, the treating respiratory or allergy specialist was asked whether the patient would benefit from systematic assessment of difficult asthma and if they deemed it appropriate, they referred such patients to a difficult asthma service for a systematic assessment.

2.2. Indications for systematic assessment of difficult asthma

Referrals for systematic assessment were only accepted from respiratory and allergy specialists. This included referrals from our institution's general asthma clinic as well as from other institutions. Patients were considered to have 'difficult asthma' if the managing respiratory or allergy specialists experienced difficulty managing the patients due to one or more of the following: a) diagnostic dilemma; b) poor symptom control; c) frequent or serious exacerbations; d) poor lung function; e) patient factors complicating management or f) other reasons (to be defined by the referrer). We deliberately kept the inclusion criteria broad to reflect the real-life difficulties faced by asthma specialists.

2.3. Characterization of difficult asthma through systematic assessment

Consecutive patients with difficult asthma who underwent systematic assessment between 1st June 2014 and 30th November 2015 were then included for analysis. These patients were referred from our institution's general asthma clinic both during and after the 3 month audit period, as well as from external institutions throughout the 18 month study period. All patients had extended lung function, questionnaires for asthma control and comorbidity detection, protocolized medical review, asthma phenotyping, patient education, and a panel discussion by at least three consultants.

Variable airflow obstruction was documented by: bronchodilator reversibility of the forced expiratory volume in one second (FEV_1) of greater or equal to 12%, and greater or equal to 200 ml following administration of 400mcg of salbutamol; or positive bronchoprovocation with mannitol; or >12% variability on peak flow charting over 2 weeks. Symptom control was assessed using the Asthma Control Test (ACT). This is the sum of 5 questions relating to asthma symptoms and asthma reliever use over the last 4 weeks. The score ranges from 5 to 25, with a higher score reflecting better asthma control. A score of less than 20 indicates poor control, and a score of less than 16 indicates extremely poor control [14]. Quality of life was measured with the Asthma Quality of Life Questionnaire (AQLQ). The AQLQ score is the mean of 32 disease specific quality of life questions. Four domains including symptoms, activity limitation, emotional function and environmental stimuli are assessed. A lower AQLQ represents greater impairment of health status [15]. Asthma exacerbations requiring treatment with systemic corticosteroids, and asthma-related hospitalization in the prior 12 months were recorded.

Severe asthma was defined according to the American Thoracic Society/European Respiratory Society (ATS/ERS) criteria: 1) requirement for high intensity asthma medication (GINA treatment Step 4–5) and 2) uncontrolled asthma. Asthma was considered uncontrolled if symptom control was poor (ACT<20), exacerbations were frequent (2 or more bursts of systemic corticosteroids in the previous year), there was a history of serious exacerbation the previous year (requiring hospital admission or ICU stay), or the presence of airflow limitation (pre-bronchodilator <80% and FEV1/FVC less than lower limit of normal).

The eosinophilic phenotype was considered present if absolute blood eosinophil count was greater than 0.3×10^9 cells/L and/or if the fraction of exhaled nitric oxide (FeNO) was greater than 35 ppb (using a Medisoft Hypair device, Medisoft, Sorinnes, Belgium). The presence of atopy was based on positive skin prick test to a standard panel of aeroallergens or demonstration of positive specific IgE to aeroallergens in serum. In-depth asthma and inhaler technique education was provided, as well as an action plan.

To detect pulmonary comorbidities such as chronic obstructive pulmonary disease (COPD) and bronchiectasis, chest computer