Respiratory Medicine (2014) 108, 264–270

Available online at www.sciencedirect.com

ScienceDirect

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

Asthma control in patients on fixed dose combination evaluated with mannitol challenge test☆

Kerstin A.M. Romberg [a,b,*], Anna-Carin Berggren [c], Leif Bjermer [b]

[a] Näsets Läkargrupp Falsterbovägen, Höllviken, Sweden
[b] Skane University Hospital, Department of Respiratory Medicine and Allergology, Lund, Sweden
[c] Mundipharma AB, Mölndalsvägen, Göteborg, Sweden

Received 24 September 2013; accepted 14 December 2013
Available online 22 December 2013

KEYWORDS
Beta2-agonist;
Inflammation;
Hyperresponsiveness;
ACT;
Spirometry

Summary
Asthma is often difficult to control and it is likely that not all patients are optimally treated.

This study aimed to explore asthma control in adults receiving fixed dose combination (FDC) therapy. Control of asthma was assessed using the mannitol challenge test as a monitoring tool to see if this would give additional information compared to the asthma control test (ACT). The study was an open-label, prospective study on 98 adults prescribed with FDC therapies for at least three months.

74 patients considered that their asthma was well controlled. However, 60 patients had a positive mannitol challenge test (PD15 $<$ 635 mg), and when those with a positive response to the short-acting β_2-agonist ($\geq$15%) after the mannitol challenge test were included, this increased to 64 patients (65%). Exploratory analysis determined that the spirometry parameters; FEV_1/FVC and FEV_1% of predicted, were statistically significant predictors of a positive mannitol challenge test. Co-morbid conditions such as concomitant upper airway involvement or eczema did not predict mannitol reactivity.

Although most patients rated their asthma as well controlled, many provided a positive mannitol challenge test, suggesting the presence of underlying inflammation, despite treatment with fixed dose combination therapy.

☆ This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-No Derivative Works License, which permits non-commercial use, distribution, and reproduction in any medium, provided the original author and source are credited.

* Corresponding author. University Hospital of Lund, Department of Respiratory Medicine and Allergology, Lund, Sweden. Tel.: +46 (0) 708 470 514.
E-mail address: kro@nlg.nu (K.A.M. Romberg).

0954-6111/$ - see front matter © 2013 The Authors. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.rmed.2013.12.005

This study indicates that many asthma patients on fixed dose combination therapy may not be optimally treated.
© 2013 The Authors. Published by Elsevier Ltd. All rights reserved.

Introduction

Asthma is one of the most common chronic diseases in Sweden with a prevalence of about 8% in the adult population [1]. The strategy for treating asthma depends on what level of disease the patients have. A common medication for treating asthma is a fixed dose combination (FDC) of an inhaled corticosteroid with a long acting β_2-agonist. The FDC's available at the time of the study were budesonide/formoterol (Symbicort®, AstraZeneca), fluticasone/salmeterol (Seretide®, GlaxoSmithKline) and beclometasone/formoterol (Innovair®, Chiesi).

Achieving and managing good control over asthma is difficult. Adherence to therapy is a recognized problem. Moreover, it is clear that spirometry and lung function tests are not sufficient objective methodologies for the detection of uncontrolled disease with ongoing inflammation in the entire part of the lower airways. Here we tested the hypothesis that not all asthma patients are optimally treated.

In the present study, we explored the prevalence of optimally treated asthma patients in primary care consecutively attending at a single site in Sweden. Several different strategies were employed to evaluate the degree of clinical control over the asthma of real-life patients. These included spirometry, symptom questionnaires and a bronchial provocation test (mannitol challenge test). The mannitol challenge test is an indirect assessment that reflects ongoing disease in asthma with the added advantage that it provides information on disease activity and can be used to guide treatment decisions [2].

Methods

Study design and patient population

This was an open-label study conducted at one primary care site in Sweden. The main objective of the study was to evaluate the real-life effectiveness of FDC asthma therapy. To participate in the study, patients had to have a previously verified asthma diagnosis, aged 18—65 years, and been prescribed any FDC therapy available on a regular basis for at least three months and were not allowed to have taken oral corticosteroids within the 28 days leading up to the study. Enrolled patients were required to have a forced expiratory volume in the first second (FEV_1) of at least 70% of the predicted value according to the recommendations in the Summary of Product Characteristics (SmPC) for mannitol. Patients with other respiratory or obstructive disease, including recent infection or exacerbation, were excluded from the study.

Consecutive patients, attending their appointments at the primary care site, were enrolled at a first visit for evaluating eligibility according the inclusion criteria. Eligible patients were asked to continue with their usual asthma medication until the second visit, which was up to 4 weeks later. However, the patient's normal FDC asthma therapy was to be withheld in the morning of visit 2. This was due to the observational study design, which was designed not to interfere with the patient's ordinary medication except during the day of the test. At the second visit the inclusion criteria had to be confirmed again before the asthma control test (ACT) and mannitol challenge test were performed. After the mannitol challenge test a reversibility test was performed. Following asthma evaluation, the patient's usual asthma therapy was continued as normal.

All patients provided written informed consent before participation. The study was approved by a local Ethics Committee and was conducted in accordance with the International Conference on Harmonization legislation of Good Clinical Practice (ICH GCP), the declaration of Helsinki, and all applicable regulatory requirements.

Asthma assessments

The ACT is an advocated tool to estimate clinical control [3]. The asthma severity of each participant was assessed two-fold: (1) Patients rated their own disease-control in the ACT; (2) The Investigator rated the frequency of symptoms experienced each week. The ACT was rated on a scale of 0—25, where scores of 20—25 signified good asthma control (well-treated) and scores below 20 indicated that the patient felt symptomatic.

Asthma severity was assessed by evaluating the medication each patient was prescribed by their usual physician. The Investigator also classified the frequency of symptoms experienced by the patient as A: No symptoms; B: Symptoms 1—2 times per week; C: Symptoms 3—6 times per week and D: Daily symptoms.

Mannitol challenge and reversibility tests

Oral mannitol inhalation powder (Aridol®/Osmohale®) is a well-characterized indirect bronchial challenge test suitable for use in a primary-care setting [4]. It is also standardized, reproducible and correlate to the degree of inflammation in the airways. The mannitol challenge test was performed by step-wise administering the mannitol dry powder by inhalation in increasing doses (0, 5, 10, 20, 40, 80, 160, 160 and 160 mg mannitol with cumulative doses of 0, 5, 15, 35, 75, 155, 315, 475 and 635 mg mannitol in total at each administration). A direct positive test was defined as the cumulative dose $\leq$635 mg inducing a drop in FEV by $\geq$15% (PD15 FEV). Between each dose, the bronchial hyperresponsiveness of each patient was measured by spirometry. The challenge test was positive if the FEV_1 fell

Download English Version:

https://daneshyari.com/en/article/6242317

Download Persian Version:

https://daneshyari.com/article/6242317

Daneshyari.com