Comparison of two budesonide powder inhalers, Easyhaler® and Turbuhaler®, in steroid-naïve asthmatic patients

H. Schweisfurth*, A. Malinen†, T. Koskela, P. Toivanen‡, M. Ranki-Pesonen§, on behalf of the German Study Group.

Abstract The objective of this multicenter study was to compare the clinical efficacy, safety, and acceptability of Easyhaler® and Turbuhaler® for the delivery of budesonide 200 μg/dose twice daily in steroid-naïve asthmatic patients. Three hundred and twenty-six newly diagnosed, steroid-naïve adult patients with mild-to-moderate asthma were recruited into this randomized, double-blind, double-dummy, parallel-group study, comprising a 2-week run-in period and 8 weeks of treatment. Patients received budesonide inhalation powder 400 μg/day either via Easyhaler® (n = 159) or via Turbuhaler® (n = 167), plus salbutamol inhalation powder (100 μg/dose) via Easyhaler® as rescue therapy. The study was completed by 292 patients: 143 in the Easyhaler® group and 149 in the Turbuhaler® group. The primary outcome variable, mean morning peak expiratory flow (PEF), improved significantly and almost similarly by 36.3 and 30.6 l/min, respectively, from run-in to weeks 7–8. At weeks 7–8, the mean (±SE) difference in morning PEF between the two treatments was 7.1 (±9.4) l/min (90% CI from −8.4 to 22.6) on per protocol analysis, which was within the defined limits for therapeutic equivalence. There were no significant differences between treatments in terms of secondary efficacy variables or adverse events. However, patients found Easyhaler® more acceptable than Turbuhaler®. The results show that budesonide via Easyhaler® is clinically as effective as Pulmicort® Turbuhaler® when equal daily doses of budesonide are delivered to steroid-naïve asthmatic patients. Moreover, patients found Easyhaler® more acceptable than Turbuhaler®, and a majority would prefer Easyhaler® if given a choice.

INTRODUCTION

Current national and international guidelines for the treatment of patients with asthma recommend the early use of regular anti-inflammatory therapy with inhaled corticosteroids. These agents have potent local activity: they decrease the accumulation and activation of inflammatory cells in the asthmatic lung (1), inhibit the release of inflammatory mediators from effector cells (2), and upregulate β2-receptor function (3). As a result, they decrease microvascular permeability and mucus formation (4,5).

Clinical studies have provided extensive evidence that, irrespective of preparation, inhaled corticosteroids have minimal systemic effects at doses up to 400 μg/day in children and up to 800 μg/day in adults (6). The most common adverse drug reactions of inhaled corticosteroids are dysphonia and oral candidiasis (7). Budesonide is a non-halogenated glucocorticoid derivative and is widely documented in the treatment of bronchial asthma (8).

It is generally acknowledged that the inhaler is a key element in determining the effectiveness of asthma therapy (9). The earliest form of inhaler was the pressurized metered dose inhaler (pMDI), which remains widely used in asthma management (10). However, many patients have difficulty using this device correctly (11) because of difficulty in co-ordinating drug release and inspiration (12). In addition, pMDIs contain lubricants that may irritate the bronchial membrane, resulting in paradoxical
bronchoconstriction (13). Furthermore, the most commonly used propellant (chlorofluorocarbon (CFC)) has been implicated in damage to the ozone layer, hence CFC-containing MDIs will be banned in the near future.

In order to overcome these problems, breath-actuated powder inhalers were developed. One of the first multidose powder inhalers to become available was Turbuhaler® (AstraZeneca, Sweden), which is documented for the delivery of budesonide in asthma patients as Pulmicort® Turbuhaler® (14-17). The environmental problems caused by CFC gases in pMDIs are circumvented by the introduction of budesonide and Turbuhaler® (20). Additional advantages of Easyhaler® include a dose counter, high dosing accuracy, insensitivity of fine particle dose to inspiratory flow rate, and ease of use (20).

Easyhaler® and Turbuhaler® have been shown to deliver an equivalent fine particle dose in vitro (21), with a comparable in vivo lung deposition of Tc-labeled budesonide (22). The present study was undertaken to compare the clinical efficacy, safety, patient acceptability and tolerability of Easyhaler® and Turbuhaler® for the delivery of budesonide 200 μg/dose twice daily in steroid-naïve asthmatic patients.

MATERIALS AND METHODS

Patients

Adult asthmatic out-patients who had been diagnosed with bronchial asthma no more than 2 years previously were recruited into the study from 30 centers in Germany. Inclusion criteria were: age 18–70 years; non-smokers for at least 6 months prior to entry (maximum smoking history of one pack per day for 5 years); a forced expiratory volume in 1s (FEV1) 60–90% of the predicted value measured within 4 weeks before or during the first visit; additionally, at least one of the following criteria 4 weeks before first visit or during the first visit:

(a) At least 15% increase in FEV1 or PEF after a sympathomimetic inhalation (200–400 μg salbutamol, 500–1000 μg terbutaline or 200 μg fenoterol).
(b) At least 15% decrease in FEV1 after an exercise tolerance test.
(c) At least 20% diurnal variability in PEF on at least 4 days during 1 week, based on the following formula (23):

\[
\text{Diurnal variabaility} = \frac{\text{Highest PEF} - \text{Lowest PEF}}{\text{Highest PEF}} \times 100.
\]

Exclusion criteria were: hypersensitivity to budesonide or lactose; any exacerbation of asthma or a respiratory infection during the preceding 4 weeks; hospitalization due to asthma during the previous 12 months; treatment with inhaled or systemic corticosteroids, sodium cromoglycate or nedocromil within 12 weeks before the first visit or for more than 30 days per year during the previous 5 years; manifest heart condition (NYHA Class II–IV); severe hepatic or renal disease; inadequately controlled hyperthyroidism; chronic bronchitis; diabetes mellitus (type I or II); any clinically significant deviation in safety laboratory parameters. Women were excluded if they were pregnant or breastfeeding or, if fertile, without reliable contraception. All patients who had participated in this or any other clinical trial within 8 weeks prior to study entry were also excluded.

Study design and treatments

This study was carried out according to a randomized, double-blind, double-dummy, parallel-group design. After a 2-week run-in period during which all patients used salbutamol Easyhaler® (Buventol Easyhaler® 100 μg/dose, Orion Pharma, Finland) as needed, patients were randomized to receive 200 μg of budesonide either via Easyhaler® (Giona® Easyhaler® 200 μg/dose, Orion Pharma, Finland) or via Turbuhaler® (Pulmicort® Turbuhaler® 200 μg/dose, AstraZeneca, Sweden) twice daily (at 0600–0800 and 1900–2100 hours) for 8 weeks (Fig. 1). Those patients randomized to receive budesonide via Easyhaler® concurrently inhaled placebo (lactose) via Turbuhaler® and vice versa. The appearance and weight of placebo was indistinguishable from the active treatment. Patients were instructed to rinse their mouth with water and spit it out after inhalation of each drug. The patients were trained to use both inhalers properly according to the manufacturer’s instructions. The inhaler technique was also checked during the control visits, which took place at 2-week (visits 1–4) and 4-week (visit 5) intervals.

Salbutamol Easyhaler® could be used as rescue medication during the treatment period but preferably not during the 6 h prior to home PEF measurements or follow-up visits to the clinic for spirometry. Patients were also permitted to take a 1-week course of an oral corticosteroid if needed, but any further use resulted in withdrawal from the study.

All study documents were reviewed and approved by the Ethics Committee of the Landesärztekammer Bran-
denburg, Germany. All patients were required to give written informed consent and the study was conducted according to the principles of the current revision of the Declaration of Helsinki (24).

**Outcome variables**

The primary efficacy variable was morning PEF measured at home. Daily morning (0600–0800 hours) and evening (1900–2200 hours) PEF was measured by the patient at home using a standard Vitalograph Peak Flow Meter (Vitalograph, Cat. No. 43.000G, Hamburg). Three successive exhalations were recorded and the best value was used for the final analysis. Mean PEF values were calculated for the run-in period and for treatment weeks 1–2, 3–4 and 7–8. Secondary efficacy variables consisted of evening PEF measured at home; FEV₁ and FVC measured at follow-up visits; number of salbutamol inhalations per day during the treatment period; severity scores for asthma symptoms during the day and night; visual analog scale (VAS) scores for efficacy, as determined by the patients and the investigators; and diurnal PEF variability.

The intensity of asthma symptoms (dyspnea, wheeze and cough) was scored daily by the patients and entered onto their diary cards, where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms. Patients were asked to specify whether the symptoms occurred during the day or night or early morning.

Both patients and investigators evaluated the efficacy of the treatment with a 100 mm VAS, ranging from ‘not efficient’ (0 mm) to ‘very efficient’ (100 mm). These evaluations were performed after the run-in period and after 8 weeks of treatment.

Patients were asked to record the occurrence of any adverse event into the diary. In addition, the investigator inquired on each visit whether patient had had any untoward medical events since last visit. The investigators performed a visual examination for oropharyngeal candidiasis at each follow-up visit. Morning (0700–0900 hours) serum cortisol measurements were performed before and after the treatment period to evaluate the possible effect of budesonide on the HPA axis.

Patent acceptability of the devices was determined after 4 weeks of treatment using a questionnaire consisting of 10 questions, and a VAS, ranging from ‘very poor’ (0 mm) to ‘very good’ (100 mm).

**Statistical analysis**

The overall hypothesis tested in the study was therapeutic equivalence of Giona® (budesonide) Easyhaler® and Pulmicort® Turbuhaler®. This was defined as a 90% confidence interval within ±30 l/min for estimated treatment difference in mean morning PEF during treatment weeks 7–8. Additional hypotheses were that improvement in morning PEF could be detected during treatment with Budesonide Easyhaler®, and that treatments with Budesonide Easyhaler® and Pulmicort® Turbuhaler® were equally safe, tolerable and acceptable. A two-sided P value of <0.05 was considered statistically significant if not otherwise stated.

For the primary efficacy variable (morning PEF measurements), data were analyzed on both an intention-to-treat (ITT) and a per protocol (PP) basis. Secondary efficacy variable data were analyzed only on an ITT basis. Data from all patients entered into the study were analyzed for safety and acceptability.
Therapeutic equivalence was analyzed using analysis of covariance (ANCOVA). Improvement in the Easyhaler® group was analyzed using analysis of variance (ANOVA). Spirometry values were analyzed with a repeated measurements ANCOVA model, while the number of salbutamol inhalations per day, intensity scores for asthma symptoms, VAS scores for efficacy and diurnal PEF variation were analyzed as change from run-in to treatment weeks 5–8. VAS scores for device acceptability were compared using the Wilcoxon signed rank test.

Safety analyses included morning serum cortisol using the ANCOVA model, and adverse events, which were classified by System Organ Class and by preferred term according to the WHO coding system. Oropharyngeal candidiasis was analyzed descriptively.

RESULTS

Patients

A total of 326 patients were recruited into the study from 30 centers in Germany: 159 in the Easyhaler® group and 167 in the Turbuhaler® group. Demographic and baseline features of all patients in each treatment group are shown in Table 1. There were no statistically significant differences between the groups for any of the specified parameters.

Table 1. Demographic and baseline patient information. Values are means (sd) except for sex, number of atopics, number of patients with FEV1 <80% of predicted, and number of patients demonstrating the inclusion criteria (a)–(c).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Easyhaler® n = 159</th>
<th>Turbuhaler® n = 167</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41 (14)</td>
<td>43 (13)</td>
</tr>
<tr>
<td>Female/male</td>
<td>102/57</td>
<td>101/66</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170 (9)</td>
<td>167 (9)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73 (15)</td>
<td>76 (17)</td>
</tr>
<tr>
<td>Duration of asthma symptoms (years)</td>
<td>0.4 (0.7)</td>
<td>0.5 (0.7)</td>
</tr>
<tr>
<td>Number of atopics</td>
<td>46</td>
<td>54</td>
</tr>
<tr>
<td>Morning PEF (l/min)</td>
<td>356 (103)</td>
<td>358 (110)</td>
</tr>
<tr>
<td>Evening PEF (l/min)</td>
<td>366 (104)</td>
<td>367 (112)</td>
</tr>
<tr>
<td>FEV1&lt;80% Of predicted</td>
<td>76.6 (12.8)</td>
<td>76.7 (13.0)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>3.00 (0.82)</td>
<td>2.99 (0.80)</td>
</tr>
<tr>
<td>% Of predicted</td>
<td>78.5 (14.9)</td>
<td>79.0 (14.5)</td>
</tr>
<tr>
<td>(a) At least 15% increase in FEV1 or PEF after a sympathomimetic inhalation</td>
<td>98</td>
<td>110</td>
</tr>
<tr>
<td>(b) At least 15% decrease in FEV1 after exercise-tolerance test</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td>(c) At least 20% diurnal variability</td>
<td>18</td>
<td>22</td>
</tr>
<tr>
<td>At least two of the criteria above (a–c)</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>None of criteria above (a–c) due to a screening failure or missing data</td>
<td>2</td>
<td>—</td>
</tr>
</tbody>
</table>

*Baseline FEV1 and FVC values are from measurements performed at visit 1, at the beginning of the run-in period.

Two hundred and ninety-two patients completed the study: 143 in the Easyhaler® group and 149 in the Turbuhaler® group. Sixteen patients in the Easyhaler® group and 18 patients in the Turbuhaler® group discontinued the study for various reasons (Table 2).

Table 2. Reasons for study discontinuation

<table>
<thead>
<tr>
<th>Reason</th>
<th>Easyhaler® group</th>
<th>Turbuhaler® group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse event</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Efficacy</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Loss to follow-up</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Protocol violation</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Withdrawal of consent</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>—</td>
</tr>
</tbody>
</table>

Efficacy

According to both the PP and ITT analyses, mean morning PEF improved significantly from baseline (run-in) to weeks 7–8 with both preparations, with a mean (sd) increase of 36.3 (6.6) l/min in the Easyhaler® group and 30.6 (5.7) l/min in the Turbuhaler® group on PP analysis (Fig. 2, Table 3). At weeks 7–8, the mean (se) difference
in morning PEF between the two treatments was 7.2 (9.4) l/min (90% CI from -22.6 to 22.6) on PP analysis and 7.0 (9.0) l/min (90% CI from -21.9 to 21.9) on ITT analysis, which was within the defined limits for therapeutic equivalence. The effect of sympathomimetic use on treatment difference was analyzed separately by excluding the patients who had used the rescue medication regularly. The result of this analysis did not differ from the original result.

Evening PEF values improved in accordance with morning PEF values, with a mean (SE) improvement from baseline to weeks 7-8 of 32.2 (5.7) l/min in the Easyhaler group and 27.9 (5.4) l/min in the Turbuhaler group.

Spirometric indices also improved to a similar extent in both treatment groups over the study period (Table 4). Between the end of run-in and the final visit at week 8, the mean (sd) improvement in FEV₁ was 0.2 (0.5) l in the Easyhaler group and 0.2 (0.5) l in the Turbuhaler group. Similarly, the mean (sd) improvement in FVC was 0.2 (0.6) and 0.3 (0.7) l for the Easyhaler and Turbuhaler groups, respectively. The corresponding change in mean FEV₁ as percent predicted was 5.1 (15.6) % points in the Easyhaler group and 7.5 (15.3) in the Turbuhaler group (treatment difference -0.06 with a 95% CI from -0.22 to 0.09). The change in mean FVC as percent predicted was 4.8 (16.4) % points in the Easyhaler group and 7.2 (18.3) in the Turbuhaler group (treatment difference -1.21 with a 95% CI from -4.85 to 2.43).

Use of rescue medication decreased during the study in both treatment groups. In the Easyhaler group, the mean (SD) number of salbutamol inhalations per day decreased from 1.8 (2.2) during the run-in period to 0.7 (1.3) during treatment weeks 5-8 (p<0.001). In the Turbuhaler group, the corresponding figures were 1.5 (2.2) and 0.6 (1.0) (p<0.001), respectively.

The incidence of asthma symptoms was higher during the run-in period than during the treatment period and was similar in both treatment groups (between treatments, weeks 5-8: day symptoms p=0.83, night symptoms p=0.74) (Table 5). Mean nighttime symptom scores were lower than mean day-time symptom scores in both groups. There were also no statistically significant differences between the treatments in terms of efficacy based on VAS scores by investigator (p=0.61) or patient (p=0.58), which improved during the course of the study in both groups. Mean (sd) VAS efficacy scores, as assessed by patient, increased by 24.4 (28.0) mm in the Easyhaler group and by 21.7 (28.3) mm in the Turbuhaler group, giving mean (sd) VAS efficacy scores at the end of treatment of 78.2 (16.7) and 77.5 (17.0) mm in each group, respectively.

Diurnal variability in PEF values decreased to a similar extent in both treatment groups. Thus, mean (sd) diurnal variability in PEF changed from 7.3 (4.4) % during run-in to 5.2 (4.3) % during weeks 7-8 in the Easyhaler group, and from 7.4 (5.0) to 5.5 (4.4) % in the Turbuhaler group.

Acceptability
The mean (sd) VAS score for device acceptability was significantly higher for Easyhaler than for Turbuhaler

### Table 3
Mean (SD) Changes in Spirometry (FEV₁ and FVC) Values (L) from the End of Run-in to Week 8

<table>
<thead>
<tr>
<th></th>
<th>Easyhaler</th>
<th>Turbuhaler</th>
<th>Treatment difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁</td>
<td>2.62 (0.70)</td>
<td>2.80 (0.76)</td>
<td>-0.18 (-0.33 to -0.02)</td>
</tr>
<tr>
<td>FVC</td>
<td>3.09 (0.88)</td>
<td>3.28 (0.93)</td>
<td>-0.19 (-0.34 to -0.05)</td>
</tr>
</tbody>
</table>
Easyhaler® also scored higher than Turbuhaler® for most questions in the device acceptability questionnaire (Fig. 3). In particular, patients using Easyhaler® found it easier to know when the drug had been received, and how much drug remained in the device. Furthermore, 63.8% patients said they would have chosen Easyhaler® compared with 12.4% who preferred Turbuhaler® and 22.8% who expressed no preference.

Safety
Adverse events that were considered possibly or probably related to study treatment occurred in 3.1% of Easyhaler® patients during both the first and the second half of the treatment period. In the Turbuhaler® group, 4.8% of patients experienced such events during the first half of treatment and 2.4% during the second half of treatment. Overall, 12 adverse drug reactions (ADRs) were reported in the Easyhaler® group and 16 in the Turbuhaler® group. Most of these were mild or moderate in nature. Dysphonia (3 and 4 events, respectively) and pharyngitis (4 and 5 events, respectively) were the most common reported ADRs.

Four patients withdrew from the study as a result of adverse events: one in the Easyhaler® group (irritation of the oral mucosa and throat) and three in the Turbuhaler® group (bacterial bronchitis; dyspnea and cough; and deterioration of asthma).

Only two SAEs occurred during the study, neither of which was considered related to study treatment. These consisted of one neoplasm (cervical carcinoma) in the Easyhaler® group and one respiratory system disorder (hospitalization because of dyspnoea and urinary tract infection) in the Turbuhaler® group.

In the Easyhaler® group mean (SD) morning serum cortisol value was 424 (219) nmol/l after run-in, and slightly higher at visit 8 (443 (191) nmol/l). In the Turbuhaler® group, the trend was similar (from 368 (187) to 419 (194) nmol/l). At the end of treatment, only seven patients had serum cortisol values below the reference range (138–690 nmol/l) (25): one in the Easyhaler® group and six in the Turbuhaler® group. The number of oral, 1-week steroid courses was three in the Easyhaler® group and one in the Turbuhaler® group.

### Table 5. Mean day- and night-time symptom scores (% of theoretical maximum) during run-in and treatment weeks 5–8

<table>
<thead>
<tr>
<th></th>
<th>Easyhaler®</th>
<th>Turbuhaler®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>Week 5–8</td>
<td>Week 5–8</td>
</tr>
<tr>
<td>Morning</td>
<td>22.3</td>
<td>20.8</td>
</tr>
<tr>
<td>Night</td>
<td>11.1</td>
<td>13.1</td>
</tr>
<tr>
<td>Week 5–8</td>
<td>11.1</td>
<td>16.6</td>
</tr>
<tr>
<td>Cough</td>
<td>12.1</td>
<td>7.8</td>
</tr>
<tr>
<td>Night</td>
<td>8.3</td>
<td>10.0</td>
</tr>
</tbody>
</table>

**Fig. 3.** Acceptability of the device according to questionnaire (% patients).
DISCUSSION

The results of this study demonstrated that Giona\textsuperscript{R} (budesonide) Easyhaler\textsuperscript{R} is as effective as Pulmicort\textsuperscript{R} Turbuhaler\textsuperscript{R} when equal daily doses of budesonide are delivered to steroid-na\textsuperscript{ve} asthma patients. This was evident from measurements of pulmonary function; diurnal PEF variability; asthma symptom scores; number of salbutamol inhalations per day; and VAS scores for efficacy.

The design of this study was carefully considered to ensure the optimal conditions for a rigorous comparison of the efficacy of two budesonide inhalers: Giona\textsuperscript{R} Easyhaler\textsuperscript{R} and Pulmicort\textsuperscript{R} Turbuhaler\textsuperscript{R}. Firstly, since inhaled corticosteroids may take days or weeks to exert their maximal effect, the recommended minimum duration for this type of study is 4 weeks (26). Hence, in the present study an 8-week treatment period was selected in order to obtain a reliable assessment of the efficacy, safety and acceptability of the devices under investigation. In addition, the dosage of budesonide used in this study (400 \(\mu\)g/day) is low compared with the average starting dose in adults (27,28) and should be in the steep part of the budesonide dose–response curve (7), thus, enhancing the reliability of comparison between the two preparations investigated. The inclusion of a separate placebo control group was considered to be unethical in this population of newly diagnosed, untreated asthmatic patients. Joyce et al. studied the placebo effect in a meta-analysis of 33 asthma drug therapy trials (29). According to their observations, a mean absolute decrease of 2.24 l/min in PEF was observed among placebo groups, which supports the rationale for not including a placebo group in our study.

During the trial, the primary efficacy variable and all secondary efficacy variables improved clearly during treatment and to a similar extent in both groups. An improvement in PEF of similar magnitude has been reported in previous studies with corticosteroids in steroid-na\textsuperscript{ve} asthmatic patients (15,19).

The safety and tolerability of the two preparations was good, and was comparable between the two treatment groups. The frequencies of adverse events (whether considered potentially drug-related or not) were also similar with both treatments, with no significant effect on the HPA axis. Although morning serum cortisol is not an ideal method for assessing such an effect, because of large diurnal variation, a single blood sample is the only practical method for determination of serum cortisol in a large, multicenter study of this type.

Tests to assess the acceptability of the devices revealed a clear preference for Easyhaler\textsuperscript{R} by a majority of patients. In all, 10 questions on the questionnaire, Easyhaler\textsuperscript{R} was considered at least as good as Turbuhaler\textsuperscript{R}, and 63.8% of patients said they would prefer Easyhaler\textsuperscript{R}, given the choice. Moreover, Easyhaler\textsuperscript{R} scored statistically significantly better than Turbuhaler\textsuperscript{R} on the VAS test for acceptability. While evaluating the acceptability results it should be noticed that patients had a somewhat more thorough experience of the Easyhaler\textsuperscript{R} device than of the Turbuhaler\textsuperscript{R}, because salbutamol Easyhaler\textsuperscript{R} was used as a rescue medication in both groups. However, the findings of this study are supported by the meta-analysis of nine Easyhaler\textsuperscript{R} clinical studies, which showed that the majority of patients (60%) preferred Easyhaler\textsuperscript{R} to Turbuhaler\textsuperscript{R}, and found Easyhaler\textsuperscript{R} easier to use (64%) than Turbuhaler\textsuperscript{R} (20).

The questionnaire also revealed that a majority of patients found it easier to know when the drug had been received with Easyhaler\textsuperscript{R} (69.3%), compared with Turbuhaler\textsuperscript{R} (2.1%). This finding is likely to reflect an additional benefit of incorporating a small amount (8 mg) of lactose to the budesonide dry powder, which is used to ensure a high level of dose reproducibility (20). The amount of lactose is sufficient for the patient to detect, but below the level likely to cause a reaction in lactose intolerant patients (30).

CONCLUSIONS

The results of this study indicate that Giona\textsuperscript{R} (budesonide) Easyhaler\textsuperscript{R} is as effective as Pulmicort\textsuperscript{R} Turbuhaler\textsuperscript{R} when equal daily doses of budesonide are delivered to steroid-na\textsuperscript{ve} asthma patients. The mean improvement in morning the primary efficacy variable (PEF) seen in both treatment groups was statistically significant. There were no significant differences between the treatment groups in terms of any of the secondary efficacy variables. Similarly, there were no clinically significant differences in terms of adverse events between the study groups, and these were mostly mild or moderate in nature. Neither treatment suppressed the HPA axis, as determined by morning serum cortisol values. Both VAS testing and the use of a questionnaire demonstrated better patient acceptability of Easyhaler\textsuperscript{R} compared with Turbuhaler\textsuperscript{R}. In addition, the majority of patients said that they would choose Easyhaler\textsuperscript{R}.

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REFERENCES


27. Guidelines on the management of asthma. Statement by the British Thoracic Society, the British Paediatric Association, the Research Unit of the Royal College of Physicians of London, the King’s Fund Centre, the National Asthma Campaign, the Royal College of General Practitioners, the General Practitioners in Asthma Group, the British Association of Accident and Emergency Medicine, and the British Paediatric Respiratory Group. *Thorax* 1993; 48 (Suppl): S1–S24.

