

Eformoterol Turbohaler[®] compared with salmeterol by dry powder inhaler in asthmatic children not controlled on inhaled corticosteroids

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The aim of the study was to compare the efficacy of the inhaled long-acting β_2 -agonists eformoterol and salmeterol when added to existing inhaled corticosteroid (ICS) therapy in symptomatic asthmatic children. This randomized, 12-week, parallel-group study, performed in a primary care setting, included 156 children and adolescents (aged 6–17 years) with moderate persistent asthma. Patients were randomized to open-label eformoterol (Oxis[®]) Turbohaler[®] 9 μ g (delivered dose) or salmeterol Accuhaler[®] 50 μ g, both b.i.d, added to current ICS. Assessments included: changes in daytime reliever β_2 -agonist therapy (primary variable), total 24-h reliever use, lung function, clinic and diary symptom scores, patient and carer health-related quality of life (HRQL) and adverse events. Daytime reliever use decreased significantly ($p < 0.001$) from baseline by 65% and 52%, respectively in the eformoterol and salmeterol treatment groups. Compared with salmeterol, eformoterol produced a greater decrease in daytime (–0.46 inhalations/day; $p = 0.081$) and 24-h (–0.70 inhalations/day; $p = 0.043$) reliever use. The percentage of patients who did not require any reliever medication during the study was significantly higher in the eformoterol group ($p < 0.05$ vs. salmeterol at weeks 8 and 12). Clinic and diary card peak expiratory flow and symptom measures all improved from baseline in both treatment arms. There was a significantly greater effect in favour of eformoterol for the reduction in clinic-assessed overall night-time symptoms ($p < 0.05$ vs. salmeterol). Clinically relevant improvements in patient-assessed HRQL occurred during treatment with eformoterol and salmeterol, but carer-assessed HRQL was improved to a clinically relevant extent, only with eformoterol. Both treatments were well tolerated. In children and adolescents with moderate persistent asthma, add-on therapy with eformoterol was well tolerated and at least as effective as salmeterol.

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In the UK, asthma is thought to affect as many as one in seven children aged 2–15 years (1). A significant proportion of asthmatic children report missing time from school (48%) (2), and many miss Physical Education lessons (45%) or have playtime disrupted (34%) because of asthma symptoms (3). This is contrary to the

aims of the Global Initiative for Asthma (GINA) guidelines, which emphasize the importance of taking control of asthma (4).

Inhaled corticosteroids (ICS) are the cornerstone of asthma treatment and are used to control the underlying inflammatory response. ICS are generally very effective in maximizing

control in children, but high usage of short-acting β_2 -agonists as relief medication and the limitations experienced as a result of asthma suggest that, for some children, low-to-moderate doses of ICS alone are insufficient to achieve optimal asthma control. Current guidelines suggest adding an inhaled β_2 -agonist with a long duration of action [eformoterol (Eformoterol is known as formoterol in some countries), salmeterol] to ICS in poorly controlled patients, including children (4, 5), as a stepwise approach to asthma treatment. This strategy may be particularly appropriate in children in preference to increasing the ICS dose, as it is recommended that only the minimum effective dose of ICS should be used in this age group (6).

Eformoterol and salmeterol have a duration of action of at least 12 h (7) and both drugs have been shown to have similar efficacy in adults with asthma (8). In contrast to salmeterol, eformoterol also has a rapid onset of bronchodilation within 3 min (7). Although eformoterol is well established for maintenance use in adults (9, 10) at doses including 4.5 μ g (delivered dose) and above, it has been licensed for paediatric use in the UK, only at the higher dose of 9 μ g (12 μ g metered dose) once or twice daily. In one placebo-controlled study in 68 children of mean age 11.9 years with moderate-to-severe asthma, some not receiving concomitant ICS, eformoterol 9 μ g was found to deliver twice the bronchodilating effect of salmeterol 50 μ g 12 h post-dose; this was achieved without any increase in systemic effects relative to salmeterol throughout the 12-h assessment period (11).

The present randomized, active comparator study, the FACT (FACT study: eformoterol vs. salmeterol: reduction in short-acting bronchodilator usage in asthmatic children treated with inhaled steroids) study, is the first to examine the clinical efficacy and safety of eformoterol compared with salmeterol in children receiving regular ICS. Standard efficacy measures chosen were consistent with those used routinely in a primary care setting, with peak expiratory flow (PEF) as the only measure of lung function. Additional emphasis was placed on assessing the impact of treatment on health-related quality of life (HRQL) for both patients and their carers.

Materials and methods

Study design

This was an open, randomized, parallel-group comparator study of 12-week duration. Patients were recruited in 56 general practice centres in

the UK and two in the Republic of Ireland. The study was performed in accordance with the Declaration of Helsinki and was approved by local Ethics Committees; all patients and (where applicable) parents/carers gave written informed consent. No placebo arm was included in this study as it was considered unethical to withhold medication approved by asthma guidelines from patients identified as needing additional treatment.

The primary objective was to compare the efficacy of twice-daily eformoterol (Oxis[®]) Turbohaler[®] (Turbohaler[®] is known as Turbuhaler[®] in some countries) and salmeterol Accuhaler[®] as second-line, controller therapy in children with asthma. Secondary objectives were to compare changes in the patients' HRQL and their parents'/carers' HRQL during treatment. The nature and frequency of adverse events (AEs) associated with eformoterol and salmeterol were also assessed.

Patients

The study was based in general practice surgeries and recruited outpatients, aged 6–17 years, with a clinical diagnosis of moderate, persistent asthma according to GINA criteria (4). To be included, patients had to have been receiving ICS for asthma at a constant dose for ≥ 4 weeks prior to enrolment, be currently using inhaled short-acting β_2 -agonists for relief of asthma symptoms (chest tightness, cough, wheeze, shortness of breath or activity-induced), and have had asthma symptoms occurring on ≥ 3 days or nights out of the past 7 days prior to enrolment. For randomization, patients needed to have continued to experience asthma symptoms as above during the run-in period and to have used ≥ 7 actuations of short-acting β_2 -agonists in the last 7 days or nights for relief of asthma symptoms.

Principal exclusion criteria were: PEF < 50% of predicted, asthma symptoms requiring immediate treatment, significant concurrent disease or health problems, or a requirement for additional medication (e.g. β -blocker therapy, nebulized therapy, oral steroids or oral short-acting β_2 -agonists) which may have interfered with the evaluation of the study drug.

Methods

The study began with a run-in period of 7–10 days, with patients receiving their regular ICS and short-acting β_2 -agonists but no study medication. This period was used to establish baseline values, to ascertain the need for

long-acting β_2 -agonist therapy and to allow training in completion of diary card and HRQL questionnaires [the Paediatric Asthma Quality of Life Questionnaire, PAQLQ, (12), and the Paediatric Asthma Caregiver's Quality of Life Questionnaire, PACQLQ, (13), completed by the patient and the same parent/carer, respectively].

Run-in was followed by the second clinic visit (visit 1 occurred at the start of the run-in) and randomization to either eformoterol Turbohaler 12 μ g b.i.d. (9 μ g delivered dose) or salmeterol Accuhaler 50 μ g b.i.d. Study medication was sourced from commercially available stock and was repackaged and administered according to a computer generated randomization scheme provided by the sponsor (Astra-Zeneca, UK).

Patients and their carers completed questionnaires and diary cards on which symptoms and PEF values were recorded on a daily basis. Subsequent clinic visits occurred after 4, 8 and 12 weeks of treatment. Drugs were self-administered by oral inhalation; patients continued to receive their current ICS and short-acting β_2 -agonists throughout the study.

At each clinic visit, inhaler technique, lung function, asthma symptoms, AEs, medication changes and HRQL changes were recorded.

Primary outcome variable. This was the comparison of treatments via diary card assessment of changes in daytime short-acting β_2 -agonist use during the 7 days prior to the final (week 12) clinic visit.

Secondary outcome variables. Patient-reported variables were obtained from diary cards; outcomes consisted of differences between treatments in 24 h and night-time as-needed short-acting β_2 -agonist use, morning and evening PEF, and overall symptom scores (daytime and night-time symptoms of chest tightness, cough, wheeze and shortness of breath, scored 0 = none, 1 = mild, 2 = moderate, 3 = severe); a question was also answered morning and evening on how the asthma made the patient feel (0 = happy, 1 = OK, 2 = sad).

The following asthma control variables were recorded: poorly controlled days (days with a PEF $\leq 80\%$ of baseline values, or where short-acting β_2 -agonists were used on ≥ 4 inhalations above baseline, or where night-time awakenings occurred because of asthma), mild exacerbations (two consecutive poorly controlled days), severe exacerbations (a requirement for oral corticosteroid treatment as judged by the investigator, or morning or evening PEF $< 70\%$ of baseline)

and time to asthma control (i.e. median time to three consecutive symptom-free days).

The impact of asthma on days absent from school or days unable to conduct physical activity were recorded, together with details of the parents'/carers' inability to perform normal activities or attend work because of their child's asthma.

At all visits, the investigator assessed symptoms and clinic PEF. Symptoms and HRQL were also determined from patient and parent/carer questionnaires. The patient questionnaires covered three domains (symptoms, activities and emotions), summarized by an overall score calculated as the mean score over all questions. The parent/carer questionnaires covered only the domains of activities and emotions together with an overall score.

Statistical analysis

The sample size calculation was based on an estimated difference between treatments of 0.5 (± 1.0 SD) inhalations of short-acting β_2 -agonist per day during week 12 of treatment; 128 evaluable patients would be needed to detect this difference at the 5% level with 80% power using the two-sample *t*-test. Allowing for a withdrawal rate of 10% during treatment and a randomization of 70% of patients enrolled, it was estimated that 205 patients needed to be enrolled in the study.

All patients who took at least one dose of study medication and had at least one clinic assessment of efficacy or at least 7 days of diary card data after randomization were included in the analysis. The change in daytime, night-time and 24-h short-acting β_2 -agonist use from run-in to 12 weeks was analysed by analysis of covariance; survival analysis (time to asthma control, time to first severe exacerbation) was compared by the log-rank test; changes in other diary variables and HRQL scores were analysed by the Wilcoxon rank sum test; the percentage of patients experiencing severe exacerbations during the 12-week treatment period was compared by a chi-squared test; clinic PEF and clinic symptoms were analysed by Wilcoxon tests; the frequency of mild exacerbations and poorly controlled days was analysed by Poisson regression; the percentage using no short-acting β_2 -agonist was analysed by chi-squared test, with the last school week before clinic visits extrapolated to the last 5 days of complete data to allow for school holidays. The influence of patient age and daily dose of inhaled steroid on change in daytime short-acting β_2 -agonist use was analysed by

analysis of covariance. All significance tests were two-sided and $p < 0.05$ was taken to represent statistical significance.

Results

Patients

The number of patients enrolled was 208, of whom 156 were randomized (eformoterol: 80; salmeterol: 76). One patient (eformoterol group) was excluded from the analysis because of insufficient assessment of efficacy after randomization. One hundred and twenty-three patients completed the study (eformoterol: 59; salmeterol: 64). Demographic and baseline characteristics are summarized in Table 1.

Thirty-three patients discontinued after randomization (eformoterol: 21; salmeterol: 12), of whom eight discontinued because of deteriorations in asthma (eformoterol: five; salmeterol: four), and six because of AEs (eformoterol: four; salmeterol: one). Compliance (at least 75% of doses of study medication taken) was similar in

both groups (eformoterol: 90% of patients; salmeterol: 88%).

Efficacy

As needed β_2 -agonist use. Both eformoterol and salmeterol significantly reduced short-acting β_2 -agonist use at all time points from run-in. At week 12, the reductions were 65% vs. 52%, for eformoterol and salmeterol, respectively for daytime use and 66% vs. 49% respectively for 24-h use. The difference between treatments in favour of eformoterol for the primary variable (daytime short-acting β_2 -agonist use), was -0.46 inhalations/day ($p = 0.081$) and, for 24-h use, -0.70 inhalations/day ($p = 0.043$) (Table 2). The increase in the proportion of patients who were reliever-free when at school also favoured eformoterol over salmeterol and was statistically significant ($p < 0.05$) at all time points (Fig. 1). Significantly more patients treated with eformoterol were able to stop taking short-acting β_2 -agonists altogether during week 8 and week 12 compared with patients treated with salmeterol [17% more at week 8 (95% CI 1%, 33%), $p = 0.043$ and 18% more at week 12 (95% CI 1%, 35%), $p = 0.040$, Fig. 1].

As needed β_2 -agonist use by subgroups. There was no evidence that age group was significantly associated with the change in daytime short-acting β_2 -agonist use after 12-week treatment. The percentage decrease from baseline in reliever use in eformoterol-treated patients was consistent in both the 6–11-year age group (64%) and 12–17-year age group (67%); the corresponding effect of salmeterol in the younger patient group was 47% and, in the 12–17-year age group, 57%. A significant association with the efficacy of both drugs and the dose of ICS was observed ($p < 0.01$). Patients receiving <400 $\mu\text{g/day}$ ICS showed a greater reduction in daytime reliever use from baseline (74% and 67% for eformoterol and salmeterol, respectively) compared with those patients receiving ≥ 400 $\mu\text{g/day}$ ICS

Table 1. Patient demographic and baseline characteristics

	Eformoterol	Salmeterol
No. of patients	79	76
Age (years) mean $\pm$ SD	11.7 $\pm$ 3.0	11.8 $\pm$ 2.8
Age group: n (%)		
6–11 years	40 (51)	41 (54)
12–17 years	39 (49)	35 (46)
Male: n (%)	50 (63)	38 (50)
Height (cm) mean $\pm$ SD	148.3 $\pm$ 18.8	148.7 $\pm$ 15.3
Weight (kg) mean $\pm$ SD	44.0 $\pm$ 17.4	48.0 $\pm$ 19.5
Current inhaled steroid dose ($\mu\text{g/day}$)		
mean $\pm$ SD	382.6 $\pm$ 241.3	341.1 $\pm$ 165.4
Range	100–1600	100–800
Run-in use of short-acting β_2 -agonist: mean $\pm$ SD (proportion of patients)		
Inhalations/night	0.84 $\pm$ 1.06 (74/79)	0.85 $\pm$ 0.88 (74/76)
Inhalations/day (not at school)	2.27 $\pm$ 1.53 (73/79)	2.41 $\pm$ 1.51 (76/76)
Inhalations/day (at school)	0.95 $\pm$ 1.20 (64/79)	1.38 $\pm$ 1.05 (70/76)
Inhalations/24 h	3.69 $\pm$ 2.48 (71/79)	4.22 $\pm$ 2.40 (74/76)
PEF at randomization	317.5 $\pm$ 110.4	311.5 $\pm$ 109.2
(l/min) mean $\pm$ SD		

PEF, peak expiratory flow.

Table 2. Changes in short-acting β_2 -agonist use from run-in to week 12

Short-acting β_2 -agonist use	Eformoterol (mean $\pm$ SD)	Salmeterol (mean $\pm$ SD)	Adjusted mean difference† (95% CI)	p-value
Daytime short-acting β_2 -agonist use (inhalations/day)	$-1.85 \pm 1.90^*$	$-1.72 \pm 2.02^*$	-0.46 ($-0.97, +0.05$)	0.081
Night-time short-acting β_2 -agonist use (inhalations/night)	$-0.56 \pm 0.83^*$	$-0.39 \pm 0.69^*$	-0.17 ($-0.42, +0.09$)	0.251
24-h short-acting β_2 -agonist use (inhalations/24 h)	$-2.45 \pm 2.29^*$	$-2.05 \pm 2.50^*$	-0.70 ($-1.37, -0.03$)	0.043

* $p < 0.001$ for change from run-in.

†The estimate of the difference between treatments for change in daytime and 24-h short-acting β_2 -agonist use is obtained from the analysis of covariance model and is adjusted for differences in run-in values.

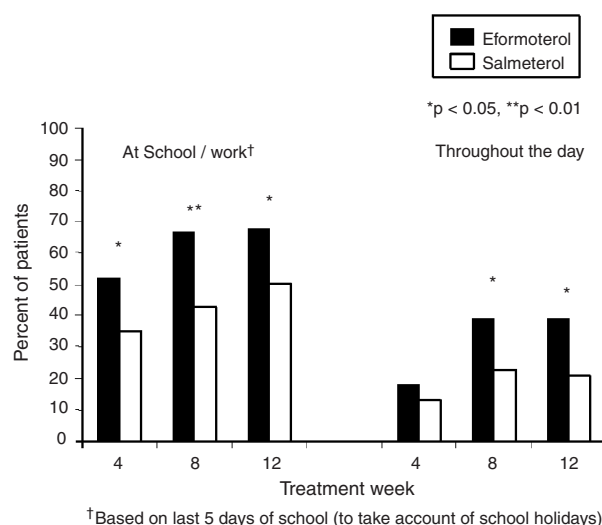


Fig. 1. Percentage of patients free of as-needed short-acting β_2 -agonists as a result of maintenance treatment with long acting β_2 -agonists.

(59% and 44% for eformoterol and salmeterol, respectively).

Lung function and symptoms. Patients in both treatment groups showed significant improvements over time in clinic PEF at 4, 8 and 12 weeks from run-in ($p < 0.01$ at all time points) (Fig. 2). These benefits were consistent with daily values of morning and evening PEF reported in the patient diaries (Table 3). Significant improvements from run-in were also observed in all diary card symptom assessments

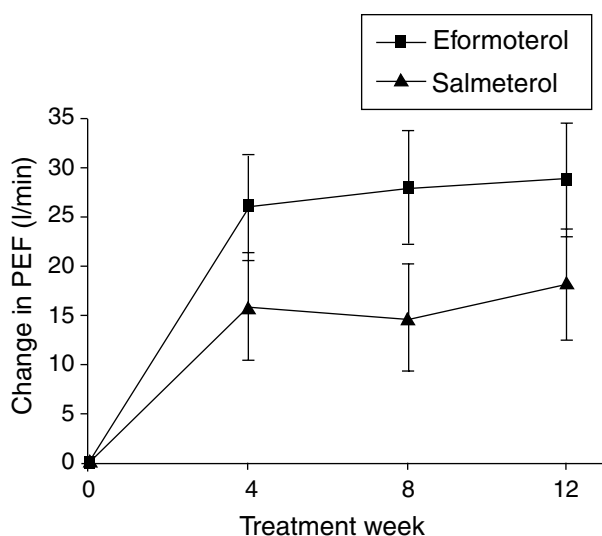


Fig. 2. Change in clinic peak expiratory flow ($\pm$ SEM) following the introduction of maintenance treatment with long acting β_2 -agonists.

and overall clinic visit measures of symptoms at week 12 for both treatment groups (Table 3). The only significant difference between treatment groups was noted in favour of eformoterol for the reduction in overall night-time symptoms assessed at the clinic ($p = 0.049$), with a trend to improvement with eformoterol in patient-reported daytime symptoms ($p = 0.052$).

Asthma control variables. Compared with salmeterol, patients treated with eformoterol reported a 27% lower frequency of poorly controlled days (12.4 vs. 17.0/patient/12 weeks, ratio 0.73; $p = 0.107$) and 37% fewer mild exacerbations (7.8 vs. 12.2/patient/12 weeks, ratio 0.63; $p = 0.051$) (Fig. 3). Eformoterol-treated patients also tended to have a shorter median time to achieve the pre-defined criteria for asthma control (12 days vs. 26 days) although this difference was not significant ($p = 0.175$). The percentage of patients experiencing a severe exacerbation by 12 weeks was similar in both treatment groups (17%). Based on diary card data, there was no significant difference between treatments in the effect of asthma symptoms on school attendance (1–2% of days in both treatment groups), but patients taking eformoterol tended to have fewer days in which asthma interfered with their ability to join in activities (eformoterol: mean of 7.5% of days unable to join in; salmeterol: 12.5%; $p = 0.178$). The proportion of days in which parents of children taking eformoterol were unable to attend work or participate in leisure activities because of their child's asthma also tended to be lower with eformoterol (0.76% of days vs. 3.52% with salmeterol; $p = 0.071$).

Health-related quality of life

Patients' HRQL was significantly improved, relative to scores at run-in at all time points ($p < 0.01$) as revealed by the PAQLQ, with clinically important improvements of 0.5 being shown in the overall score and in all domains in both treatment arms; however, there was an overall trend towards greater improvements with eformoterol (Fig. 4). Parent-assessed HRQL (revealed by the PACQLQ) also showed clinically relevant improvements in the overall score and each domain with eformoterol, with a significant difference in favour of eformoterol ($p = 0.017$) in the activity domain (Fig. 4). In contrast, salmeterol failed to improve parent HRQL or the activity of parents, as assessed by the PACQLQ, sufficiently to achieve clinical relevance (0.5 units).

Table 3. Changes in secondary efficacy variables from run-in to week 12

Variable	Eformoterol (mean $\pm$ SD)	Salmeterol (mean $\pm$ SD)	Mean treatment difference (95% CI)	p-value
PEF (l/min)				
Morning	+33.8 $\pm$ 53.0**	+20.8 $\pm$ 34.5**	+13.0 (–1.6, +27.6)	0.198
Evening	+28.0 $\pm$ 52.1**	+19.0 $\pm$ 30.0**	+9.0 (–4.8, +22.7)	0.564
Clinic PEF (l/min)	+28.8 $\pm$ 50.5**	+18.1 $\pm$ 48.6**	+10.7 (–5.0, +26.4)	0.355
Patient overall asthma symptom severity score (0–3)				
Daytime	–0.70 $\pm$ 0.62**	–0.53 $\pm$ 0.57**	–0.17 (–0.36, +0.02)	0.052
Night-time	–0.50 $\pm$ 0.59**	–0.47 $\pm$ 0.62**	–0.02 (–0.22, +0.17)	0.687
Clinician overall asthma symptom severity score (0–3)				
Daytime	–0.74 $\pm$ 0.88**	–0.61 $\pm$ 0.82**	–0.12 (–0.40, +0.15)	0.324
Night-time	–0.75 $\pm$ 0.94**	–0.51 $\pm$ 0.85**	–0.24 (–0.52, +0.05)	0.049
Limited activity days because of asthma (days/week)	–0.92 $\pm$ 2.03**	–0.66 $\pm$ 1.91*	–0.26 (–0.90, +0.39)	0.622
Night-time awakenings because of asthma (nights/week)	–1.03 $\pm$ 1.96**	–1.31 $\pm$ 1.94**	+0.28 (–0.36, +0.92)	0.632
Patient overall feeling about asthma symptoms (0–2)				
During day	–0.45 $\pm$ 0.59**	–0.39 $\pm$ 0.49**	–0.06 (–0.24, +0.11)	0.288
During night	–0.36 $\pm$ 0.52**	–0.32 $\pm$ 0.51**	–0.03 (–0.20, +0.14)	0.954

* $p < 0.01$, ** $p < 0.001$ for change from run-in.

PEF, peak expiratory flow.

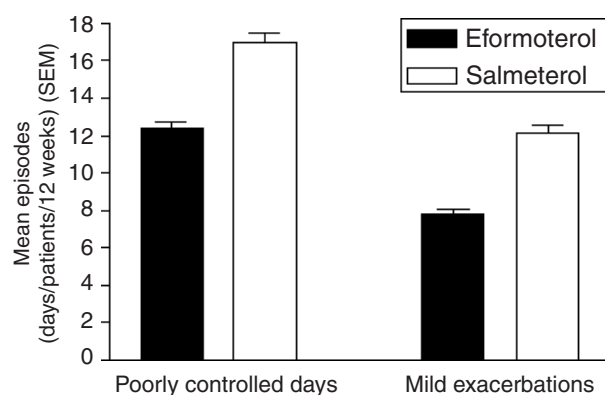


Fig. 3. Frequency of asthma control problems during maintenance treatment with long acting β_2 -agonists.

Safety

During the treatment period, AEs were reported by 44 of 80 (55%) of patients receiving eformoterol and by 45 of 76 (59%) patients receiving salmeterol. The number, nature and intensity of AEs were the same for both treatments, with the most common AEs being headache (eformoterol 14, salmeterol 17), asthma aggravation (eformoterol eight, salmeterol 10) and upper respiratory tract infection (eformoterol seven, salmeterol nine). Two patients reported serious AEs, testicular torsion (eformoterol) and diabetes mellitus (salmeterol), but neither were considered related to test treatment.

Discussion

The FACT study compared the clinical efficacy of eformoterol Turbohaler with salmeterol

Accuhaler in children and adolescents aged 6–17 years with moderate persistent asthma.

Eformoterol was shown to be at least as effective as salmeterol based on the primary endpoint, with both treatments reducing the need for short-acting β_2 -agonists in line with improved asthma control as recommended by the GINA guidelines (4). There were significant differences in favour of eformoterol in some secondary endpoints: total short-acting β_2 -agonist use, per cent of patients free from as-needed β_2 -agonist use at school and throughout the day and overall nocturnal symptoms assessed at the clinic; the difference in mild exacerbations approached significance (a 37% reduction in favour of eformoterol; $p = 0.0509$). In addition, the extent of parental activity limitation due to their child's asthma was also decreased significantly with eformoterol compared with salmeterol, based on the PACQLQ. The doses studied were chosen because they are the doses approved for children, not because they are therapeutically equivalent and this could explain why eformoterol showed or tended towards superiority over salmeterol according to several measures.

As expected, lung function improved significantly from baseline in both treatment groups, with notable numerical differences between the two treatments in favour of eformoterol (~13 l/min increase) for clinic PEF and morning PEF. The confidence intervals for the treatment difference suggest that eformoterol is at least as effective a bronchodilator as salmeterol. However, as salmeterol has been shown to improve PEF by 8–16 l/min vs. placebo or salbutamol in other studies with asthmatic children (14–17), this incremental improvement in morning PEF

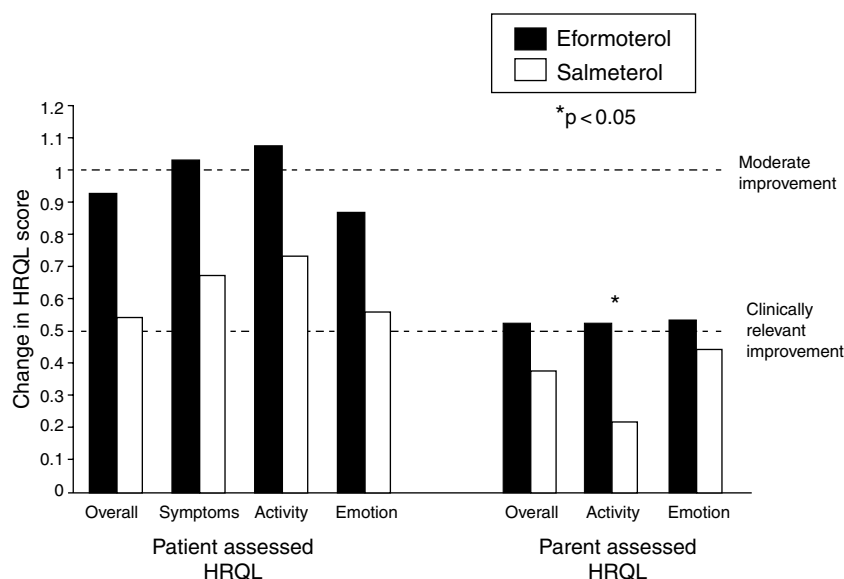


Fig. 4. Health-related quality of life improvements from run-in after 12 weeks maintenance treatment with long acting β_2 -agonists.

with eformoterol (34 l/min vs. 21 l/min) may be of clinical relevance. Indeed, a recent placebo-controlled study has demonstrated that eformoterol 9 μ g and salmeterol 50 μ g in children are not equivalent, as an increase in forced expiratory volume in 1 s (FEV₁) of 7% was observed with eformoterol over salmeterol that lasted for at least 12 h when these doses were compared (11).

One of the limitations of this study was the lack of a placebo arm; although this was considered, it was excluded for ethical reasons as all patients required additional treatment at entry. It was also considered technically too difficult to adopt a double-dummy study design, as this would have required young children to use two study inhalers and two existing inhalers. The primary and secondary endpoints in this study were intended to be clinically relevant to primary care physicians and less reliant on requiring specialist lung-function equipment (e.g. spirometers to assess FEV₁). This meant that most of the efficacy data were recorded in patient diaries. Clinic PEF was recorded along with several clinic assessments of symptom control and HRQL. In addition, while most studies with salmeterol in children have concentrated on measuring only lung function, this study examined as-needed β_2 -agonist use and HRQL as important indicators of maximum applicability to the patient and their parent or carer.

The consistent treatment benefits on all pre-defined endpoints, both subjective and objective, indicate the advantages of using inhaled long-acting β_2 -agonists in combination with ICS in children with persistent asthma symptoms – as has been consistently shown with adults in, for example, the FACET (9) and OPTIMA (10)

studies. However, it has been claimed that the added benefit of these drugs in children is less than in adults (18) based on studies of salmeterol in children with mild, persistent asthma (19, 20). The results of our study, the first to compare two long-acting β_2 -agonists in children, clearly confirm the value of both eformoterol and salmeterol in children with moderate, persistent asthma that is not well controlled by low-to-moderate doses of inhaled steroids. Furthermore, our results do not suggest that the two test treatments can be considered equivalent for all efficacy parameters: eformoterol shows significant advantages over salmeterol for several endpoints and, for the primary endpoint in particular, some suggestion of a greater advantage for eformoterol was seen in the younger children and in those requiring higher steroid doses. More studies are warranted to examine if the efficacy differences between eformoterol and salmeterol in this study can be confirmed – particularly in younger children and children with poor asthma control who should have greater capacity for showing improvement.

Both treatments were well tolerated and there was no evidence of tolerance to the efficacy of either drug; both drugs should be considered a viable option for add-on therapy to ICS in children with asthma to optimize asthma control and to improve HRQL for both patients and their carers.

Conclusions

Eformoterol and salmeterol reduced as-needed β_2 -agonist use and provided clinically important improvements in symptoms and HRQL in paediatric

diatric and adolescent patients with symptomatic moderate persistent asthma. Eformoterol was at least as efficacious and equally well tolerated as salmeterol in childhood asthma.

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