Effect of salmeterol on respiratory muscle activity during exercise in poorly reversible COPD

W D C Man, N Mustfa, D Nikoletou, S Kaul, N Hart, G F Rafferty, N Donaldson, M I Polkey, J Moxham

Background: Some patients with irreversible chronic obstructive pulmonary disease (COPD) experience subjective benefit from long acting bronchodilators without change in forced expiratory volume in 1 second (FEV1). Dynamic hyperinflation is an important determinant of exercise induced dyspnoea in COPD. We hypothesised that long acting bronchodilators improve symptoms by reducing dynamic hyperinflation and work of breathing, as measured by respiratory muscle pressure-time products.

Methods: Sixteen patients with ‘irreversible’ COPD (<10% improvement in FEV1, following a bronchodilator challenge; mean FEV1: 31.1% predicted) were recruited into a randomised, double blind, placebo controlled, crossover study of salmeterol (50 µg twice a day). Treatment periods were of 2 weeks duration with a 2 week washout period. Primary outcome measures were end exercise isotime transdiaphragmatic pressure-time product and dynamic hyperinflation as measured by inspiratory capacity.

Results: Salmeterol significantly reduced the transdiaphragmatic pressure-time product (294.5 ± 348.6 cm H2O/s/min; p = 0.03), dynamic hyperinflation (0.22 ± 0.33 litres; p = 0.002), and Borg scores during endurance treadmill walk (3.78 ± 4.62; p = 0.02). There was no significant change in exercise endurance time. Improvements in isotime Borg score were significantly correlated to changes in tidal volume/oesophageal pressure swings, end expiratory lung volume, and inspiratory capacity, but not pressure-time products.

Conclusions: Despite apparent ‘non-reversibility’ in spirometric parameters, long acting bronchodilators can cause both symptomatic and physiological improvement during exercise in severe COPD.
dosed inhaler) and no infective exacerbation in the preceding 6 weeks. The King’s College Hospital research ethics committee approved the protocol and all participants gave informed written consent.

**Study design/medications**

The study was of a randomised, double blind, placebo controlled, crossover design with a run in period of 2 weeks and consisted of five outpatient visits. On visit 1, subjects performed full baseline lung function tests, including formal bronchodilator reversibility, and incremental shuttle walks to determine predicted peak oxygen consumption (V\text{O}_{2}\text{peak}). Patients stable on inhaled corticosteroids remained on this medication throughout the trial. All other medications apart from rescue short acting \( \beta_2 \) agonists were stopped at the start of the run in period between visits 1 and 2; patients with a symptomatic exacerbation or spirometric deterioration during the run in period were withdrawn from the study and restarted on their usual medication. During both visits 1 and 2 subjects were familiarised with treadmill walking and the performance of inspiratory capacity manoeuvres at rest and during treadmill walking. At the end of visit 2 subjects were randomised to receive either placebo followed by salmeterol (50 \( \mu \)g) twice a day or salmeterol followed by placebo using a computer generated randomisation schedule, the Patient Allocation for Clinical Trials. Treatments were given via matching metered dose inhalers and spacer for 2 weeks with a 2 week washout period between visits 3 and 4. Post-treatment measurements were made on visits 3 and 5 at the same time of day for each patient. The study medication (salmeterol or placebo) was taken 2 hours before lung function tests and 3 hours before the exercise tests. In terms of “rescue therapy”, patients were allowed short acting \( \beta_2 \) agonists during treatment periods, but these were stopped for at least 8 hours before measurements were made.

**Exercise tests**

On visits 3 and 5 an endurance treadmill test was performed, as well as spirometry and total lung capacity (TLC) obtained from body plethysmography. The chosen walking speed was that producing 80\% of predicted V\text{O}_{2}\text{peak}, with predicted V\text{O}_{2}\text{peak} calculated using a regression equation from the maximum exercise distance achieved during the baseline incremental shuttle walk at visit 1.\(^\text{11}\) Patients were given standardised encouragement at 1 minute intervals during the walking test to continue exercising until exhaustion. During the treadmill walk, flow was measured by a pneumotachograph (F300L, GM Instruments Ltd, Kilwinning, UK) and tidal volume integrated from inspiratory flow. Operational lung volumes were evaluated from measurements of inspiratory capacity (IC)\(^\text{14}\) at rest, every minute during exercise, and at end exercise, while dyspnoea was assessed by recording modified Borg scores\(^\text{15}\) at 1 minute intervals. Each patient was given a few breaths warning before each IC manoeuvre, and then verbally encouraged to make a maximal effort before relaxing. Oesophageal and transdiaphragmatic pressure swings during the IC manoeuvres were observed to ensure uniformity of maximal effort. As TLC is assumed not to change during exercise,\(^\text{14,16}\) the following operational lung volumes were calculated:

- end expiratory lung volume (EELV) = TLC – IC;
- inspiratory reserve volume (IRV) = IC – tidal volume;
- end inspiratory lung volume (EILV) = TLC – IRV.

**Respiratory muscle activity**

Oesophageal pressure (Poes) and gastric pressure (Pga) were measured at rest and during exercise using conventionally placed balloon catheters attached to differential pressure transducers (MP45, Validyne, CA, USA). Transdiaphragmatic pressures (Pdi) were obtained online by subtraction of Poes from Pga. All signals were digitised using a NB-MIO-16 analogue-digital converter (National Instruments, Texas, USA) and acquired on a Macintosh PowerMac 7600 computer running LabVIEW-4 software (National Instruments, Texas, USA). The sampling rate was 100 Hz.

Inspiratory muscle strength was assessed using volitional tests: maximum inspiratory mouth pressure (P\text{im}ax), and oesophageal and transdiaphragmatic pressures during a maximal sniff (sniff Poes, sniff Pdi) as previously described.\(^\text{14}\) The pressure-time products (PTPs) of Pdi, Poes, and Pga (PTPdi, PTPoes, and PTPga) were obtained by multiplying the area subtended by the pressure trace by the respiratory frequency and had units of cm H\text{2}O/s/min. PTPdi and PTPoes were calculated during inspiration of each breath, while PTPga was calculated during expiration (the duty cycle being defined by the appropriate zero points of flow). For PTPdi and PTPga, the baseline was determined for each breath as the level observed at the start of inspiration and expiration, respectively. As the baseline for PTPoes may be overestimated as a result of abdominal muscle action,\(^\text{17}\) this was determined for each breath by the method validated by Appendini and colleagues.\(^\text{19}\) This involved subtracting the decrease in Pga from the fall in Poes during the interval between the onset of inspiratory effort and the point of zero flow. The mean PTPs presented in the results were calculated from the PTP values obtained after analysing each individual breath in the preceding 30 seconds before isotime.

To estimate the mecanonoventilatory association of the respiratory system (a crude estimate of compliance), tidal volume divided by the difference in oesophageal pressure during points of zero flow (AVV/APOes) was calculated by breath.

**Data and statistical analysis**

Based on previous PTP data during exercise in COPD patients,\(^\text{2}\) a minimum of 15 patients were required to show a reduction of 50 cm H\text{2}O in PTPdi with 80\% power. Primary outcome measures were PTPdi and IC at end exercise isotime (ISO). ISO was the highest equivalent exercise endurance time between the two treadmill walks.

Statistical analysis was performed using SPSS 11.1 for Windows. Patients were divided into two groups according to the treatment sequence. Since this was a crossover trial, treatment effect was assessed after both period effect and treatment-period interactions had been assessed using two sample t tests. In the absence of period effect and treatment-period interaction, treatment effect was assessed with paired t tests or non-parametric equivalent depending on whether the groups were normally distributed. If a significant treatment-period interaction was found at the 10\% significance level, the treatment effect was assessed with a two sample t test, disregarding data from the second period. Univariate and multivariate regression analysis was used to compare the effect of salmeterol on isotime Borg score change with isotime lung volumes, dynamic hyperinflation, respiratory muscle activity and mechanics, as well as changes in static lung function.

**RESULTS**

Sixteen of the 20 patients completed the study; two were withdrawn because of worsening of symptoms during the run in period and two developed infective exacerbations during the treatment periods (one while on placebo and the other on salmeterol). Ten of the 16 patients received salmeterol as the first intervention. Baseline characteristics of the remaining participants are shown in table 1. Of note,
mean change in FEV\textsubscript{1} was only 10 ml following a bronchodilator reversibility test.

**Lung function and respiratory muscle strength**

Salmeterol had no significant effect on spirometric measurements or TLC, although resting hyperinflation appeared to be reduced as evidenced by a reduced RV:TLC ratio and an increased IC (tables 2 and 3). There were no changes in inspiratory muscle strength (table 2).

**Endurance treadmill exercise**

Salmeterol did not have a significant effect on tidal volume, respiratory frequency, minute ventilation, inspiratory/expiratory time, inspiratory duty cycle, or transcutaneous oxygen saturation. However, there was a significant reduction in breathlessness as measured by mean ISO Borg score from rest to isotime (table 3). In addition, salmeterol led to a significant reduction in the primary outcome measure (ISO IC), accompanied by improvements in operational lung volumes (table 3). Mean (SD) ISO IC was 0.98 (0.44) l following placebo and 1.27 (0.51) l after salmeterol (mean difference 0.29 (95% CI 0.11 to 0.44); p = 0.002).

**Respiratory muscle pressure time products (PTPs)**

Figure 1 shows the effects of salmeterol on ISO PTPs. Salmeterol led to a significant reduction in the primary outcome measure, mean (SD) ISO PTP\textsubscript{d1} (294.5 (99.6) v 348.6 (95.9) cm H\textsubscript{2}O/s/min; mean difference −54.2 (95% CI −102.5 to −5.9); p = 0.03), and also in mean ISO PTP\textsubscript{g1} (544.8 (291.3) v 659.3 (312.2) cm H\textsubscript{2}O/s/min; mean difference −115 (95% CI −225.7 to −3.5); p = 0.04).

**Improvements in isotime Borg score**

There was no significant linear relationship between improvements in ISO Borg score and changes in respiratory muscle PTP, breathing pattern, minute ventilation, or baseline lung function. However, significant linear correlations were found between changes in ISO Δtidal volume/Δoesophageal pressure (r = 0.60; p = 0.01), EELV/TLC% (r = 0.58; p = 0.02) and IC (r = 0.56; p = 0.02) and ISO Borg score (fig 2). On backwards multivariate analysis, only Δtidal volume/Δoesophageal pressure and EELV/TLC% remained significant independent factors.

**DISCUSSION**

Using a randomised, placebo controlled, double blind, cross-over design, we assessed the effects of a long acting \textsubscript{12} agonist, salmeterol, on inspiratory and expiratory muscle activity as well as dyspnoea, exercise capacity, and dynamic hyperinflation in patients with poorly reversible COPD. The principal finding is that, in the absence of a spirometric response to a bronchodilator challenge, this treatment can reduce dynamic hyperinflation and respiratory muscle activity in patients with severe COPD, suggesting a physiological basis for a reduction in symptoms.

**Significance of findings**

Recent work has emphasised the role of dynamic hyperinflation as a key determinant of exercise induced dyspnoea.\textsuperscript{8,9} Bronchodilators have also previously been shown to reduce dynamic hyperinflation during exercise in COPD. Belman and colleagues showed that a single dose of albuterol significantly reduced breathlessness and end expiratory/end inspiratory lung volumes during incremental cycle ergometry,\textsuperscript{10} while similar findings were described by O’Donnell and colleagues during endurance cycling following a 3 week period of nebulised ipratropium bromide.\textsuperscript{9} Boni and colleagues have shown a relationship between changes in resting IC following inhaled salbutamol and dyspnoea during light exercise in COPD patients with expiratory flow limitation.\textsuperscript{11}

Apart from obvious differences in design, exercise test, and therapeutic drug, our study offers important additional information compared with these previous studies. Our patients were markedly more severe (FEV\textsubscript{1} 0.76 l compared with 1.20, 1.05 and 1.75 l) and none of our patients had any spirometric response to bronchodilator challenge (mean FEV\textsubscript{1} change 10 ml compared with 110, 230 and 390 ml). Despite this, our patients showed comparable improvements in operating lung volumes during exercise with salmeterol.

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**Table 1** Baseline characteristics of study patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M:F)</td>
<td>10:6</td>
</tr>
<tr>
<td>Age (years)</td>
<td>68.1 (7.6)</td>
</tr>
<tr>
<td>Smoking history (pack years)</td>
<td>33.5 (13.8)</td>
</tr>
<tr>
<td>Pre-BD FEV\textsubscript{1} (l)</td>
<td>0.76 (0.17)</td>
</tr>
<tr>
<td>Post-BD FEV\textsubscript{1} (l)</td>
<td>0.77 (0.15)</td>
</tr>
<tr>
<td>FEV\textsubscript{1} (%)</td>
<td>31.9 (3.9)</td>
</tr>
<tr>
<td>FEV\textsubscript{1}/VC (%)</td>
<td>38.8 (14.8)</td>
</tr>
<tr>
<td>RV (%)</td>
<td>115 (14.5)</td>
</tr>
<tr>
<td>PaCO\textsubscript{2} (kPa)</td>
<td>8.7 (0.9)</td>
</tr>
<tr>
<td>PaCO\textsubscript{2} (mM)</td>
<td>5.3 (0.6)</td>
</tr>
<tr>
<td>ISW distance (m)</td>
<td>275 (72)</td>
</tr>
</tbody>
</table>

**Table 2** Effect of salmeterol on lung function and respiratory muscle strength

<table>
<thead>
<tr>
<th>Measure</th>
<th>Placebo</th>
<th>Salmeterol</th>
<th>Mean difference (95% CI)</th>
<th>Drug effect p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV\textsubscript{1} (l)</td>
<td>0.74 (0.22)</td>
<td>0.78 (0.26)</td>
<td>−0.04 (−0.40 to −0.02)</td>
<td>0.07*</td>
</tr>
<tr>
<td>VC (l)</td>
<td>2.26 (0.78)</td>
<td>2.38 (0.79)</td>
<td>−0.12 (−1.40 to −0.30)</td>
<td>0.19</td>
</tr>
<tr>
<td>FEV\textsubscript{1}/VC (%)</td>
<td>35.0 (11.5)</td>
<td>33.9 (10.1)</td>
<td>1.1 (−3.6 to 1.3)</td>
<td>0.34</td>
</tr>
<tr>
<td>TLC (l)</td>
<td>6.56 (1.47)</td>
<td>6.45 (1.44)</td>
<td>0.11 (−0.30 to 0.08)</td>
<td>0.22</td>
</tr>
<tr>
<td>RV (l)</td>
<td>4.30 (0.82)</td>
<td>4.08 (0.90)</td>
<td>0.23 (−0.48 to 0.03)</td>
<td>0.08</td>
</tr>
<tr>
<td>RV/TLC (%)</td>
<td>63.9 (0.80)</td>
<td>63.1 (0.77)</td>
<td>2.6 (−4.9 to −0.33)</td>
<td>0.03</td>
</tr>
<tr>
<td>Pmax</td>
<td>81.1 (14.5)</td>
<td>77.4 (12.2)</td>
<td>−3.7 (−9.5 to 1.2)</td>
<td>0.12</td>
</tr>
<tr>
<td>Sniff Pdi</td>
<td>99.9 (10.7)</td>
<td>97.8 (16.3)</td>
<td>−2.1 (−8.7 to 4.5)</td>
<td>0.52</td>
</tr>
<tr>
<td>Sniff Poes</td>
<td>79.6 (12.4)</td>
<td>78.8 (12.9)</td>
<td>−0.8 (−4.7 to 3.1)</td>
<td>0.66</td>
</tr>
</tbody>
</table>

Values are mean (SD) or mean treatment differences with 95% confidence intervals. Respiratory muscle strength tests are measured in cm H\textsubscript{2}O.

FEV\textsubscript{1} = forced expiratory volume in 1 second; VC = vital capacity; TLC = total lung capacity; RV = residual volume; Pmax = maximum inspiratory pressure; Pdi = diaphragmatic pressure; Poes =oesophageal pressure.

*Significant period × treatment interaction.
Dynamic hyperinflation during exercise increases EELV, leading to adverse mechanical sequelae including breathing on a higher and less steep portion of the compliance curve, as well as a positive pressure within the alveoli at the end of expiration. PEEPi acts as an inspiratory threshold load that increases the work of breathing and also places the diaphragm at a mechanical disadvantage. Although PTPdi was reduced at isotime with salmeterol, there was no significant change in PTPoes. This is not altogether surprising, given that hyperinflation is more detrimental to the rib cage or accessory inspiratory muscles. The effect on PTPga corroborates previous findings that expiratory muscle activity increases with progressive airflow obstruction and dynamic hyperinflation. Increased

Table 3  Effect of salmeterol on dyspnoea and operational lung volumes during treadmill exercise

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Salmeterol</th>
<th>Mean difference (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest Borg</td>
<td>0.0 (0.0, 0.5)</td>
<td>0.0 (0.0, 0.5)</td>
<td>0.03 (−0.17 to 0.24)</td>
<td>0.75</td>
</tr>
<tr>
<td>ISO Borg</td>
<td>4.62 (1.09)</td>
<td>3.78 (1.14)</td>
<td>−0.84 (−1.54 to −0.14)</td>
<td>0.02</td>
</tr>
<tr>
<td>∆Borg</td>
<td>4.34 (1.22)</td>
<td>3.47 (1.07)</td>
<td>−0.87 (−1.55 to −0.20)</td>
<td>0.01</td>
</tr>
<tr>
<td>Rest IC (l)</td>
<td>1.32 (0.45)</td>
<td>1.48 (0.52)</td>
<td>0.16 (0.02 to 0.32)</td>
<td>0.03*</td>
</tr>
<tr>
<td>ISO IC (l)</td>
<td>0.99 (0.44)</td>
<td>1.27 (0.51)</td>
<td>0.29 (0.11 to 0.44)</td>
<td>0.002</td>
</tr>
<tr>
<td>DH (∆IC) (l)</td>
<td>0.33 (0.20)</td>
<td>0.22 (0.15)</td>
<td>−0.11 (−0.18 to −0.04)</td>
<td>0.002</td>
</tr>
<tr>
<td>Rest EELV/TLC (%)</td>
<td>64.0 (7.7)</td>
<td>67.6 (7.7)</td>
<td>−3.4 (−6.3 to −0.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>ISO EELV/TLC (%)</td>
<td>85.0 (8.6)</td>
<td>80.3 (6.9)</td>
<td>−4.8 (−8.0 to −2.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>∆ EELV/TLC (%)</td>
<td>3.3 (3.0)</td>
<td>3.2 (2.6)</td>
<td>−0.10 (−2.7 to −0.7)</td>
<td>0.003</td>
</tr>
<tr>
<td>Rest EILV/TLC (%)</td>
<td>90.2 (6.2)</td>
<td>87.1 (6.0)</td>
<td>−3.1 (−5.6 to −0.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>ISO EILV/TLC (%)</td>
<td>99.2 (5.7)</td>
<td>93.5 (5.3)</td>
<td>−5.7 (−7.6 to −1.8)</td>
<td>0.004</td>
</tr>
<tr>
<td>∆ EILV/TLC (%)</td>
<td>8.0 (4.3)</td>
<td>6.4 (4.5)</td>
<td>−1.6 (−3.3 to 0.1)</td>
<td>0.07</td>
</tr>
<tr>
<td>ISO Saco2 (%)</td>
<td>87.0 (6.7)</td>
<td>87.8 (6.4)</td>
<td>0.8 (−0.4 to 1.9)</td>
<td>0.18</td>
</tr>
<tr>
<td>Endurance time (s)</td>
<td>333 (151)</td>
<td>347 (180)</td>
<td>14 (−23.9 to 52.0)</td>
<td>0.44</td>
</tr>
</tbody>
</table>

Values are mean (SD) and mean treatment differences with 95% CI except for resting Borg scores where values are median (25th, 75th interquartile range).

Borg = modified Borg dyspnoea scale; ∆ = change from rest to end isotime; IC = inspiratory capacity; DH = dynamic hyperinflation; EELV = end expiratory lung volume; EILV = end inspiratory lung volume; TLC = total lung capacity;
IRV = inspiratory reserve volume; ISO = isotime

*Significant period x treatment interaction.
expiratory muscle activity cannot contribute to greater
expiratory flow, and it remains unclear what role this
abdominal muscle activity plays as it should be detrimental
in energy terms.

Although salmeterol reduced isotime PTPdi and PTPga,
there was no significant linear relationship with improve-
ments in dyspnoea. The best correlates of reduced breath-
lessness were changes in operational lung volumes,
particularly EELV/TLC and IC, and in Δtidal volume/
Δoesophageal pressure. Current hypotheses on the origin
of dyspnoea emphasise the role of neuromechanical dissociation
(a disparity between the respiratory drive or motor output
and the mechanical response of the system) rather than work of
breathing per se.27 This is supported by recent work which
found a progressive mismatch between diaphragm electro-
volumes, in the absence of changes in FEV1 or breathing
strength tests, including sniff Pd.i. Alternatively, the improve-
given that no change was seen in the inspiratory muscle
response and hence decrease neuromechanical uncoupling.

One potential explanation for our findings could be
improved inspiratory muscle contractility with salmeterol as
β2 agonists may increase the maximal force generated by the
diaphragm.29 However, this is unlikely to play a major role
given that no change was seen in the inspiratory muscle
strength tests, including sniff Pd.i. Alternatively, the improve-
ments in dynamic hyperinflation and operational lung
volumes, in the absence of changes in FEV1 or breathing
pattern, suggest that salmeterol may exert its effects in the
peripheral airways—bronchodilation leading to reduced
small airways resistance.30,31

Despite the improvements in exertional dyspnoea, opera-
tional lung volumes, and respiratory muscle activity, salme-
terol did not improve endurance time. This may partly be due
to the relatively small sample size which was designed to
demonstrate significant changes in PTPdi rather than
to changes in exercise capacity. Given the invasive nature of
oesophageal and gastric balloon placement on two separate
occasions for each patient, it was not appropriate to recruit a
larger number of patients. Another possible explanation is
quadrieps dysfunction; lower limb muscle weakness is well
documented in COPD32 and quadrieps fatigue may con-
tribute to limited exercise tolerance.33,34 Saey and colleagues
have shown that endurance cycling time does not improve
following nebulised ipratropium in patients with COPD who
develop contractile quadrieps fatigue.35 However, it is
important to note that quadrieps fatigue is probably a less
significant factor during walking.36

This study has shown that, despite “non-reversibility” in
spirometry, a long acting bronchodilator can lead to
physiological improvements in patients with severe COPD.
A 2 week treatment period of salmeterol improves exertional
dyspnoea and operational lung volumes, and reduces
diaphragmatic and abdominal muscle activity. A poor
spirometric response to a bronchodilator challenge in COPD
patients does not preclude symptomatic and physiological
improvements during exercise with a long acting β2 agonist.

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estimating end-expiratory lung volume changes during exercise in patients
Budesonide/formoterol may be used for adjustable maintenance dosing in asthma

This randomised, double blind/open two phase multicentre study, sponsored by Astra Zeneca, was conducted over 7 months to find out if asthma control was better when patients adjusted the maintenance dose of inhaled budesonide/formoterol (Symbicort Turbobalser) according to asthma symptoms than when fixed dose (FD) regimens were used. Eligible patients were randomised to one of three groups: (1) Symbicort FD 160/4.5 μg, two inhalations twice daily (bd); (2) Symbicort adjustable maintenance dose (AMD) 160/4.5 μg, two inhalations bd; or (3) salmeterol/fluticasone FD (Seretide Diskus) 50/250 μg, one inhalation bd. The study consisted of three treatment periods: run in (10–14 days), double blind (1 month with either Symbicort FD or Seretide FD), and open extension (6 months). In the open extension phase, those in the Symbicort AMD arm were advised to reduce the number of inhalations to one inhalation bd or to increase the number of inhalations to four bd for at least 7 days according to the frequency of rescuer usage and nocturnal awakenings due to asthma.

Symbicort FD significantly increased FEV₁ compared with Seretide FD (p<0.05). Comparable improvements in FEV₁ were observed with Symbicort AMD and Seretide FD. Patients in the Symbicort AMD group had significantly fewer exacerbations/hospital attendances/oral steroid courses (p<0.018) and lower use of reliever medication (p<0.01) than those in the Seretide FD group. There was no difference in the number of “well controlled asthma weeks” (WCAW) between the two FD groups, but Symbicort AMD increased the odds of achieving a WCAW compared with Symbicort FD (p = 0.049).

The results suggest that FD regimens with Symbicort and Seretide provide similar levels of asthma control. Total drug usage was lower with Symbicort AMD than FD. This study reinforces the need for home management plans and empowerment of patients to manage their asthma at home.

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