Remote daily real-time monitoring in patients with COPD — A feasibility study using a novel device

Z.M. Sund, T. Powell, R. Greenwood, N.A. Jarad*

Department Respiratory Medicine, Bristol Royal Infirmary, Marlborough Street, Bristol BS2 8HW, UK

Received 25 November 2008; accepted 24 March 2009
Available online 16 April 2009

KEYWORDS
Acute exacerbations of chronic obstructive pulmonary disease (AECOPD);
Chronic obstructive pulmonary disease (COPD);
Daily electronic monitoring

Summary
New technologies have allowed remote real-time electronic recording of symptoms and spirometry. The feasibility of utilising this technology in COPD patients has not been investigated.

This is a feasibility study. The primary objective is to determine whether the use of an electronic diary with a portable spirometer can be performed by COPD patients with a moderate to severe disease. Secondary objectives are to investigate the value of this method in early detection of acute exacerbations of COPD (AECOPD).

In this 6-month study, 18 patients recorded daily their symptom score and spirometry. Data was sent on real time. AECOPD which was defined according to pre-set criteria were noted. Spirometry values and scores for health-related quality of life were compared between the start and the end of the study. Hospitalisation rate due to AECOPD was compared with a parallel period in the previous year.

On average, patients were able to record 77% of their total study days. The system detected 73% of AECOPD. In further 27% of AECOPD patients sought treatment although the change in symptoms did not meet AECOPD definition. The number of COPD-related hospitalisations significantly reduced compared to the previous year. There was a significant increase in FEV₁ and FVC from the start to the end of the study.

The remote monitoring device used in this study can be used in COPD patients. AECOPD was detected early in the majority of cases. Hospitalisation rate due to AECOPD was reduced and FEV₁ and FVC values increased during the study.

© 2009 Elsevier Ltd. All rights reserved.

Introduction

Monitoring health status in COPD patients with the view of early detection of acute exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) is one of the goals of the respiratory community. AECOPD is an important feature of
the disease. Frequent pulmonary exacerbations have been shown to cause deterioration in health status,1–3 quality of life4 and FEV1.5

The exact definition of AECOPD remains contentious although is often characterised by an increase in symptoms including cough, sputum volume/purulence and shortness of breath sufficient enough to make patients seeking help and the physicians escalating treatment.1,6–11

Failure to treat repeated AECOPD may lead to gradual decline in lung function whereas early management of AECOPD is thought to be associated with shorter duration of symptoms12 and to enhance recovery of AECOPD.13 For the management of AECOPD to happen early, patients have to present to their clinicians with increase in symptoms. Many studies, however, continue to show that many AECOPD are unreported.5,14

Educational intervention with supervision for chronic Obstructive Pulmonary Disease (COPD) patients has been shown to reduce both short- and long-term hospitalisation suggesting that an educational approach may be beneficial to patients managing their disease.15 Additionally, guided self-care by recording daily peak expiratory flow and symptoms in a paper diary has been demonstrated to reduce hospitalisations due to AECOPD.16 The use of paper diaries is suboptimal as the diagnosis of exacerbations often occurs in retrospect upon inspection of the diary.

It has been suggested that the use of an electronic diary may be a mechanism to rectifying the lack of early AECOPD reporting.17 Electronic diaries using modern communication devices enable daily recording of symptoms and spirometry to be sent to the treating clinicians on a real-time basis, thus allowing early intervention as needed.

We have previously described the value of electronic daily monitoring in cystic fibrosis (CF) and its use in understanding symptom fluctuation and early detection of acute exacerbations of CF (published in abstract form. Full manuscript is under consideration for publication at present).18 Because of the young age of CF patients, it is possible that they are able to use modern electronic methods of communication more readily than COPD patients, particularly the more elderly patients and those with advanced disease.

The current feasibility study is primarily designed to determine whether an electronic real-time remote monitoring system can be used by COPD patients with a moderate to severe disease for adequate number of days to allow monitoring of their health status and early detection of signs of AECOPD.

Patients, material and methods

Patients

This is a single centre study. All patients were recruited from the Department of Respiratory Medicine, Bristol Royal Infirmary. Southmead Research Ethics Committee, Bristol approved the study.

The inclusion criteria were: diagnosis of COPD, ≥40 years, an FEV1 < 80% predicted, FEV1/FVC < 70, 10 pack-year smoking history and free from AECOPD for 2 weeks prior to entering the study. Diagnosis of COPD was based on documented diagnosis of the diseases. Patients in whom asthma diagnosis was recorded in medical notes were excluded from the study. Patients with other reasons for obstructive defect (for example bronchiectasis) were excluded from the study.

Patients who had any co-morbidity serious enough to shorten life to less than one year in the estimate of the investigator or had undergone lung surgery were not included. Patients residing in an area with no network connectivity and/or a significant cognitive problem were also excluded. All patients were given sufficient time to read the patient information sheet and any questions were answered in advance. Patients’ General Practitioners (GPs) were informed of the study at the point of enrolment.

Study design

This was a 6-month feasibility study. At the start of the study basic demographic data, a medical history, current medications and reproducible lung function (FEV1, FVC) were recorded using a Spiro USB Spirometer (Micro Medical, UK). An AR20 quality of life questionnaire was also completed.21 At the end of the study lung function was recorded and the AR20 questionnaire was repeated. Change in FEV1 and FVC as assessed by this method, rather by patients own daily recording, was taken for analysis between the start and the end of the study.

The device

An XDa system is a mobile-enabled Personal Digital Assistant. The XDa systems used in this study were provided by O2 Telecommunication, UK and were attachable to a handheld Vitalograph (Vitalograph, Buckinghamshire — UK) with a cable designed by e-san limited, Oxford (Fig. 1A). Software written by e-san limited was installed on the XDa system which allowed patients to easily access and enter data on their symptoms as well as to record their lung function. E-san limited was taken over by t+ Medical during the study.

Each patient had a unique identifying number linked to their Subscriber Identity Module (SIM) card. When the device was handed to another patient at the end of their enrolment, the number was changed to identify the new patient.

All patients were trained upon enrolment in the study. The device was provided after patients demonstrated mastery of recording symptoms and spirometry. In addition, all patients were provided with an information sheet illustrating how to use the device and a hand held spirometer and 2 nose clips. Upon enrolment into the study, researchers were available to answer questions and a technical helpline with e-san limited or t+ Medical was available.

Daily recording of symptoms and lung function

Patients were asked to record their symptoms and spirometry once daily in the evening. Upon switching on the XDa system there was clear entry into the programme. All symptom-related questions were pre-set (Table 1, Fig. 1B).
Patients were asked to choose 1 option for each symptom using a stylet provided with the device. Grading of symptoms was adapted from the MRC questionnaire on respiratory symptoms.19

Each symptom was graded from 1 (mild) to 5 (severe). Patients were asked to choose the severity grade which best described their symptoms for that day. In addition they were asked if they visited a medical professional that day (Yes/No).
and if they had a medication change that day (Yes/No). The device then prompted patients to attach the spirometer. Spirometry was performed according to the recommendations of the British Thoracic Society/Association of Respiratory Technicians and Physiologists (BTS/ARTP) guidelines.\(^\text{20}\) Patients were asked to perform 3 spirometry attempts. If the readings differed by \(\leq 10\%\), the reproducibility criteria were met. If reproducibility was not met the patients were asked to perform additional manoeuvres. After a maximum of 5 attempts the spirometer switched itself off. The individual highest and reproducible FEV\(_1\) and FVC were selected for each patient per day. After recording FEV\(_1\) patients were asked to click ‘send’ (Fig. 1B) and the data was sent to the research centre in real time (Fig. 1C).

### Reading and managing symptoms

A website was created for the study as a collaborative effort between one of the researchers (NAJ) of the Department of Respiratory Medicine, Bristol and e-san Limited. Only, password-permitted physicians and research scientists could access to the website. A time-score plot was designed for each patient. Each symptom score and the best FEV\(_1\) value were plotted on a daily basis (Fig. 2). To establish a baseline all patients entered an exacerbation-free run-in period of 14 days where they recorded symptom score and lung function as described above. Baseline for each symptom score and FEV\(_1\) was the median and the mean value respectively of the 14-day run-in period recordings. If an AECOPD occurred during this period, the run-in period was re-started 14 days from the end of the AECOPD. Patients who had 2 AECOPD during the run-in period were excluded from the study. Once the run-in period was successfully completed the baseline automatically disappeared at the end of exacerbation.

During the study phase patients recorded symptom score, answered the medication related questions and recorded their spirometry as previously described.

AECOPD was defined using the principles of the BTS/NICE guidelines\(^\text{22}\) as “A sustained worsening of symptom score from baseline that is acute in onset”. Commonly reported symptoms are worsening of breathlessness, cough, increased sputum production and change in sputum colour. We also arbitrary considered a \(\geq 10\%\) decline in FEV\(_1\) from baseline for 2 or more consecutive days to represent an AECOPD. AECOPD was, therefore, regarded to be present if at least one of the following criteria was encountered:

1. An increase of at least 1 degree of 2 symptom scores and/or a decline in FEV\(_1\) of \(\geq 10\%\) from baseline for \(\geq 2\) successive days.
2. A patient presenting with symptoms they felt to be those of AECOPD and sought help that resulted in them being given a course of antibiotics and/or prednisolone.

When the recordings met criteria number 1 a red line appeared on the corresponding day of the patient’s time-score plot (Fig. 2) and an electronic mail message was automatically sent to the research team.

Once an AECOPD was detected a researcher telephoned the patient and offered treatment. Whether or not the treatment started was a consensus between the doctor and the patient. An AECOPD detected by the device was counted irrespective of whether or not the patient accepted escalation of treatment. Management of AECOPD differed according to the phenotype of the AECOPD. If the AECOPD was manifested with increased breathlessness, fatigue or by a decline in lung function tests, patients were advised to take prednisolone only. If these symptoms were associated with an increase in sputum volume or purulence or if the AECOPD was manifested by these 2 symptoms alone they were advised to take antibiotics as well.

The end of exacerbation was considered to have occurred when the symptom score reduced so that they no longer met the definition of AECOPD. The exacerbation red line automatically disappeared at the end of exacerbation.

All patients were provided with a 7-day oral course of antibiotics and a 14-day oral course of prednisolone. According to hospital microbiology data, amoxicillin-clavulanic acid combination (co-amoxiclav) 625 mg three times daily was the most clinically suitable antibiotic. Ciprofloxacin 500 mg twice daily was provided for penicillin-allergic patients. Prednisolone was prescribed at 30 mg once daily. The patients’ GPs were advised to replenish the medication if used. If there was difficulty obtaining medications from GPs, the research team replenished the patient’s supply.

Upon changing medications, patients recorded this on their device. In addition they completed a form provided and sent it to the research team in a pre-paid envelope notifying the team of who they visited and/or the medication change. This allowed the additional advantage of the

<table>
<thead>
<tr>
<th>Symptom Score</th>
<th>Fatigue</th>
<th>Sputum Volume</th>
<th>Sputum Colour</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Breathless after vigorous activities (e.g. gardening or cleaning)</td>
<td>So tired that you need to rest regularly</td>
<td>Less than ½ egg cup</td>
<td>Yellow</td>
</tr>
<tr>
<td>Breathless after light activities (e.g. washing)</td>
<td>Prevented from your daily home routine (e.g. shopping or working)</td>
<td>Between ½-1 egg cup</td>
<td>Greenish</td>
</tr>
<tr>
<td>Breathless after washing and dressing</td>
<td>Unable to get out of bed</td>
<td>More than an egg cup</td>
<td>Brownish</td>
</tr>
<tr>
<td>Breathless at rest or at minimal effort</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
research team to track the date of the AECOPD that the system did not detect.

**Outcome measures**

The primary objective of the study was to quantify the number of days out of the total 180 days study period in which patients were able to record their symptoms. Other objectives included 1. the number of AECOPD detected and undetected by the monitoring system, 2. change in FEV₁, FVC, AR20 score from the start to the end of the study and 3. the number of hospital admissions and length of stay for AECOPD during the study period as compared to those during a parallel 6 months in the previous year as detected from hospital records. It was not possible to compare the number of AECOPD with the same period of time in the previous year as many AECOPD were treated outside hospital and reliable data was not available.

**Statistical analysis**

Statistical analysis was aided by the Research and Development Support Unit at the Bristol Royal Infirmary. Data was analysed using SPSS statistics (version 14).
The number of hospitalisations and the number of days spent in hospital due to AECOPD between the study year and the same period of time in the parallel previous year were analysed using Wilcoxon’s Signed Ranks Test. AR20 quality of life score between the start and the end of the study was analysed in the same way. A paired t-test was also used to compare spirometric values (FEV₁ and FVC) from the start to the end of the study period. Statistical significance was set at the 5% level.

Using the rate of hospitalisation data, a sample size calculation was used to estimate the number of patients needed for a future adequately powered randomised controlled trial comparing daily monitoring with normal care.

Results

From October 2005 to August 2006, 22 consenting patients were screened, 19 were included in the study. In one patient the data could not be analysed due to a fault in the device leaving 18 patients in the study (Fig. 3). Their baseline characteristics can be seen in Table 2.

During the study, recordings were made on average in 77% of study days (range 70–92%). A total of 75 AECOPD were diagnosed out of which 55 (73%) were detected by the remote monitoring system. In 41/55 (75%) AECOPD detected by the device, the patient agreed that their increase in symptoms was sufficient for escalation of treatment. In 14/55 (25%) AECOPD detected, patients did not feel that the increase in symptoms was sufficient enough for them to seek help. Five patients had 2 or less AECOPD throughout study period. The rest had more than 2 AECOPD.

Table 3 shows details of AECOPD throughout the study period.

Conversely, in 20/75 (27%) AECOPD patients presented with symptoms who needed treatment with antibiotics and/or corticosteroids when their symptom scores on their recordings were not sufficient to meet our pre-set definition for AECOPD. Throughout the study a total of 57 courses of antibiotics and a total of 50 courses of prednisolone were taken. Table 3 shows characteristics of the AECOPD.

Out of the 75 exacerbations, 6 exacerbations were detected by decline in FEV₁ alone. In 4 patients concurred with the diagnosis and were treated by oral corticosteroids. FEV₁ returned to baseline value at the end of the treatment in all treated patients.

Data on hospitalisations due to AECOPD was obtained from reviewing patient medical notes for all patients.

### Table 2

<table>
<thead>
<tr>
<th>Description</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who used the device for 6 months</td>
<td>18</td>
</tr>
<tr>
<td>Mean age (SD) years</td>
<td>65 (9.50)</td>
</tr>
<tr>
<td>Gender (female/male)</td>
<td>6:13</td>
</tr>
<tr>
<td>Mean FEV₁ (SD) litres</td>
<td>1.04 (0.37)</td>
</tr>
<tr>
<td>Mean FEV₁ (SD) % predicted</td>
<td>36.37 (13.35)</td>
</tr>
<tr>
<td>Mean FVC (SD) litres</td>
<td>2.62 (0.64)</td>
</tr>
<tr>
<td>Mean FVC (SD) % predicted</td>
<td>71.95 (17.26)</td>
</tr>
<tr>
<td>On long acting beta2 agonists</td>
<td>18/18 (100%)</td>
</tr>
<tr>
<td>On inhaled corticosteroids</td>
<td>14/18 (77.8%)</td>
</tr>
<tr>
<td>On long acting anticholinergic agents</td>
<td>9/18 (50%)</td>
</tr>
</tbody>
</table>

FEV₁: forced expiratory volume in the first second of expiration; and FVC: forced vital capacity.

### Table 3

<table>
<thead>
<tr>
<th>Exacerbation Characteristics</th>
<th>Total number = 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exacerbations not detected by the device</td>
<td>20/75 (27%)</td>
</tr>
<tr>
<td>Exacerbations detected by the device</td>
<td>55/75 (73%)</td>
</tr>
<tr>
<td><strong>Exacerbations detected by the device</strong></td>
<td></td>
</tr>
<tr>
<td>Exacerbations detected by the device — patients concurred</td>
<td>41/55 (75%)</td>
</tr>
<tr>
<td>Exacerbations detected by the device — patients did not concur</td>
<td>14/55 (25%)</td>
</tr>
<tr>
<td>Exacerbations diagnosed by &gt;10% decline in FEV₁ only</td>
<td>6/55 (11%)</td>
</tr>
<tr>
<td>Exacerbations manifested with increase in symptom score only</td>
<td>37/55 (67%)</td>
</tr>
<tr>
<td>Exacerbations manifested with increase in symptom score and &gt;10% decline in FEV₁</td>
<td>12/55 (22%)</td>
</tr>
</tbody>
</table>

FEV₁: forced expiratory volume in the first second of expiration.
During the study period there were 6 hospitalisations (0.33 per patient) due to AECOPD, compared to 14 (0.78 per patient) in the same 6 months in the previous year, $p = 0.027$ (Fig. 4).

The median length of stay for AECOPD in the study period was 0 day (25% percentile 0 days, 75% percentile 4.5 days), compared to 4 days (25% percentile 0 days, 75% percentile 6.5 days) for the parallel period in the year prior to the study. This comparison did not reach statistical significance, $p = 0.23$ (Fig. 4).

Over the 6-month study, there was a 66-ml increase in mean FEV$_1$ from 1.04 (SD 0.37) litres to 1.107 (SD 0.37) litres $p = 0.038$. Similarly there was a 300-ml increase in FVC from 2.62 (SD 0.64) to 2.92 (SD 0.80) litres $p = 0.050$ (Fig. 5).

In contrast there was no change in the AR20 health-related quality of life score with a median score of 11 at the beginning and at the end of the study, $p = 0.946$.

Using the rate of hospitalisation as an outcome measure, a future adequately powered randomised controlled trial comparing the intervention using this method with the usual care would require a sample size of 94 patients in each study arm (total 188 patients) to achieve 80% power to detect a difference in means if these findings were to be replicated using a two-group $t$-test with a 5% 2-sided significance level.

**Discussion**

This feasibility study shows that COPD patients can use modern electronic device to monitor their symptoms and spirometry in over three quarter of study days. The device was able to detect the majority of AECOPD. For patients
included in the study, there has been a modest improvement in spirometry values at the end of the study and a reduction in hospitalisation rate but not length of stay due to AECOPD. Daily recording has not adversely affect health status. The study has several limitations — there is no control group, the number of patients is small and the duration of study is short.

AECOPD has been defined differently in different studies. An increase in two major symptoms over two consecutive days was a defining event in one study.2 This is similar to the definition used for symptom increase in our study. In another large trial24 an increase in more than one symptom for three consecutive days was used to define AECOPD. Unlike previous studies where peak flow rate was used for daily monitoring,11,12,23 FEV1 was recorded in this study.

The decline in FEV1 of 10% or more over two consecutive days was used to define exacerbation even when symptoms did not change. We recognize that it may not be an acceptable criterion for AECOPD by all clinicians and this could potentially be regarded as a limitation to this study. But this study has helped to show that AECOPD by decline of FEV1 alone occurred only in the minority of exacerbations.

We accept that defining exacerbations in future similar studies may need to be unified, but the primary objective of this study is to assess the competency and consistency of COPD patients in recording symptoms and spirometry for 6 months period.

It has previously been recommended that COPD patients need to have an increased awareness of their symptoms and should promptly start on treatment for AECOPD.1,11,12 This would reduce the health burden in COPD and could decrease the severity of AECOPD by reducing declines in lung function thereby increasing recovery rate. In our study, treatment of AECOPD was communicated to the patients upon detection and most episodes were treated.

We have 'phenotyped' AECOPD into 2 groups and designed the treatment according to symptoms. All patients took prednisolone for AECOPD but only those with increased mucous-purulent sputum took antibiotics. Phenotyping AECOPD has shown to be important in a recent study which compared the effect of long acting anti-cholinergic agent (tiotropium) with a combination of inhaled corticosteroid (fluticasone) and long acting beta2 agonists (salmeterol).14 It was apparent that although the rate of prevention of total reported and unreported AECOPD was similar in the two arms of treatment, exacerbations that were treated with oral prednisolone were prevented more effectively with a combination of salmeterol and fluticasone. On the other hand, exacerbations that required antibiotics were prevented more effectively with tiotropium.

As stated previously, most AECOPD in this study manifested with increased symptoms without a significant change in spirometry. Decline in FEV1 alone was seldom encountered as the reason for AECOPD detection. A previous report suggested that changes in FEV1 during exacerbations may be small and was not reliable for detecting AECOPD.1 Another possibility is the fact that the decrease in FEV1 lagged behind an increase in symptoms and that the prompt treatment for may have obviated the decline in FEV1.

In our study, over one quarter of patients sought treatment for AECOPD despite the fact that changes in their symptoms and lung function tests did not meet the pre-set definition of AECOPD. The number of patients in this study is not large enough to characterise patients who had low threshold of starting the treatment. A possible reason is that the change of scoring system that we adapted from the MRC respiratory questionnaire may not have been sensitive enough to detect AECOPD. Some patients may have sought help based on previous experience of symptom deterioration prior to change in symptoms meeting the pre-set definition of AECOPD. Another possibility is that upper respiratory tract symptoms such as nasal discharge and congestion, and sore throat which this system did not measure might have prompted GP visits. These symptoms were reported in other studies in a significant number of patients over the prodromal phase (7 days before onset of exacerbation) prior to AECOPD.11,23

Hospitalisation for AECOPD is not only a major healthcare cost1,25 but has been associated with a major decline in health status,1–3 quality of life4 and FEV1.5 This study shows that this intervention significantly reduced the number of hospitalisations during the study period. Despite the obvious shortcomings of comparing the rate of hospitalisations with historic data, we did the analysis as we have a reliable data on hospital admissions. Similar results were not seen in a recently published study in which a nurse-led package did not reduce hospitalisation, although was associated with reduced mortality.6 In our study, it is not possible to identify whether being part of this research or whether the early detection and treatment of AECOPD might account of this apparent reduction in hospitalisation.

This study shows that remote daily monitoring of symptoms in COPD over a 6-month period leads to a small increase in both FEV1 and FVC. This may reflect a ‘peaking’ of the efficacy of intervention at the 2–6-month point which has been reported in larger trials.27,28 Although this might be the case, we acknowledge that our study, unlike these trials, did not compare an intervention with no intervention or placebo. It has to be considered that the improvement in spirometry may reflect a true efficacy of early intervention with early treatment for most AECOPD. As in the hospitalisation rate, it is not possible at this stage to determine the cause of this improvement be it the daily monitoring, education, early therapy or simply being part of this study has the greatest effect on outcome.

An XDa system has been used in this study, but other modalities for communications equipment with the appropriate software could be used. This includes an ordinary mobile phone, an internet connection or a remote control television. In practical terms, this method could be used in selected patients and for a short or long period of time. Patients with impaired mobility, those who live in remote areas or those who are anxious of attending healthcare premises might find this technique helpful. This technique once established could be adapted to other diseases such as asthma, and congestive cardiac failure although care must be taken to prevent over treatment as a result of lower threshold of intervention.

Based on the hospitalisation rate, we have calculated that, compared to usual care, a larger randomised control trial of 188 patients is required to explore the value remote monitoring of AECOPD. If this intervention to be compared
with other interventions such as regular telephone consultations or paper diaries, a larger number of patients are needed to detect difference in hospitalisation rate. In any case, we suggest that, an adequately powered trial, is needed since interventions aimed at delaying the progression of COPD and improve access to healthcare are considered high priority areas.

Conflict of interest

The authors have no conflict of interest to declare.

Acknowledgements

Special thanks to E san and to t Medical for designing the website and for technical support for patients and researchers. The study is funded by an unconditional grant from the David Telling charitable fund. The funding source has had no involvement in the study.

References

19. Medical research council questionnaire on respiratory symptoms; 1976.