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Inhaled therapy in elderly COPD patients; time for re-evaluation?

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Abstract

Objective: chronic obstructive pulmonary disease (COPD) prevalence steadily increases with age. However, the effectiveness of inhaled therapy in the elderly COPD population has rarely been formally evaluated. We studied a group of elderly patients with COPD with a range of severity, selected from one General Practice register to measure peak inspiratory flow (PIF) and assess patient perceived benefit.

Methods: we recruited 53 randomly selected elderly patients with COPD (36 males) with a mean age of 73.5 years (range 65–89 years). The evaluation consisted of (i) information obtained from directed questions and (ii) objective measurements of the ability to generate adequate PIF for a variety of inhalers. Patients answered questions regarding ease of use, perceived benefit from and specific problems encountered with their inhaler. Three recordings of PIF were measured at varying inhaled resistances using the 'In-Check Dial'.

Results: thirty-five were classified as mild, 17 moderate and 1 severe COPD. All patients used a metered dose inhaler (pMDI), and 12 of the patients also used a dry powder inhaler (DPI). Forty six per cent of patients using a pMDI and 17% of those using a DPI rated their device difficult to use. No patient used a nebuliser. Thirty-one of the 53 patients using just a pMDI felt they were able to perceive benefit in comparison to 4 of the 12 DPI users. Even though most DPI users (10/12) had rated their inhaler as easy to use, 50% were 'unsure' as to whether they received any clinical benefit. Most patients were unable to generate sufficient inspiratory flow to use the higher resistance DPI's and patients with COPD who were able to generate adequate PIF were invariably mild. A significant negative correlation was found between age and the PIF achieved when assessed using the high resistance device setting ($R = 0.84, P < 0.0001$). Multivariate analysis showed the effect of age on PIF was independent of the disease grade.

Conclusion: elderly patients with COPD, even when in a stable clinical condition, may be unable to gain optimum benefit from their inhaler.

Keywords: COPD, peak inspiratory flow, PIF, elderly, inhalers

Introduction

Chronic obstructive pulmonary disease (COPD) has a prevalence of 7% in the general UK population and accounts for over £500 million spent each year: the majority relating to the hospital costs [1]. Consultation rates in general practice

for COPD are two to four times higher for than any other chronic disease, rising significantly with age [2].

Inhaled bronchodilator therapy is the mainstay of treatment in the management of COPD. Although available in various inhaled (metered dose inhaler [pMDI]/dry powder inhaler [DPI] or nebulised) formulations, it is the

MDI, which is most commonly prescribed [3]. Therapeutic benefit depends on adequate airway drug deposition. Inhaler technique is crucial but disappointingly this is sub-optimum in many patient groups, particularly the elderly [4].

Arthritis, weakness, poor manual dexterity and visual limitations are potential problems affecting inhaler use in the elderly [5]. Additionally, good inhaler technique is correlated with high scores on the Mini Mental Test [6,7]. A large number of studies comparing different inhalers have tended to neglect elderly patients or have extrapolated results from younger adults or patients with asthma [8].

In order to overcome these difficulties, more 'patient friendly' devices such as breath-actuated DPIs have been developed. DPIs are seen as new, innovative, more reliable and easy to use by both patients and physicians who are under substantial marketing pressure. However, in general DPIs require a higher peak inspiratory flow (PIF) than MDIs for effective drug delivery since a minimum inspiratory flow is required to disaggregate and disperse the drug powder in the inhaled air-stream [9]. There is still a paucity of data regarding the percentage of patients with COPD who can achieve the minimum PIF values required to utilise these devices satisfactorily. There are fewer studies still in the elderly.

The aims of our study therefore were to recruit an elderly population of patients with COPD, managed in General Practice, and to assess inhaler use. We divided the evaluation into: (i) information obtained from directed questions and (ii) objective measurements of the ability to generate adequate PIF for a variety of inhalers.

Methods

The patients in this study were randomly selected and consented during their attendance at either a COPD clinic or a routine appointment (non-respiratory related) at a General Practice comprising 11 medical practitioners serving 15,000 patients. All patients had been previously diagnosed with COPD with the same hand-held spirometer by the same general practitioner according to British Thoracic Society criteria [10]. Patients who consented were over the age of 65 and excluded if they had an upper respiratory tract infection within the preceding week, previous pulmonary surgery or active cardiac disease. We studied a group of 53 elderly patients with COPD (36 males) with a mean age of 73.5 (range 65–89) years. The investigator (SJ) was aware of the COPD diagnosis of the patients but blinded to the disease severity in each case and the spirometry indices were collected by the general practitioner separately.

Directed questionnaire

We read questions word for word directly to the patient and the questions related to:

- (i) Inhaler type used [pMDI, DPI, nebuliser or combination]

- (ii) Ease of use [scored from 1 to 3: easy—1, moderately difficult —2 and difficult —3]
- (iii) Perceived benefits [no benefit/ beneficial/ don't know] and
- (iv) Specific problems experienced [handling/co-ordination/ empty device awareness/other].

Patients were also asked whether they had been issued with a spacer for use with their pMDI and whether they used it regularly. The patients who used DPIs were questioned about that device.

Peak inspiratory flow determination

PIF was measured with the 'In-Check Dial' (Clement–Clarke International, Harlow, UK) a meter with selectable resistances calibrated to measure airflow thereby simulating the use of various inhaler devices. Accuracy is within 10% or 10 l/min and the repeatability is within 5 l/min [3, 11, 12]. The same investigator (SJ) tested all the patients with the 'In-Check Dial'. The order of the resistances was randomised, three measurements from Functional Residual Capacity with the patient seated were recorded for each resistance. In each case all three readings were within 5% of each other, showing good reproducibility, with the best reading recorded.

Statistics

The study was descriptive and data were summarised as mean \pm SD or mean and range. The effects of age and COPD disease severity on PIF were assessed for the 53 patients by stepwise multivariate linear regression using SAS 9 for Windows (Cary, NC, USA).

Results

All 53 patients (36 males) used a pMDI; 12 (23%) also used a DPI including a Turbohaler ($n = 7$), an Accuhaler ($n = 4$) and a Diskhaler ($n = 1$). None used a nebuliser. A spacer device had also been prescribed for 76% of patients. Thirty-five patients were classified as mild (FEV_1 50–80% predicted), 17 moderate (FEV_1 30–49% predicted) and 1 as severe COPD ($FEV_1 < 30\%$ predicted) [10]. Subdividing the patients according to age, patients with mild COPD had a mean [\pm SD] age of 72 ± 5 years compared to 79 ± 5 years for moderate COPD ($P = < 0.001$) and 80 years in severe disease (one patient).

Directed questionnaire results

The questionnaire study revealed that 46% of patients using a pMDI and 17% of those using a DPI rated its difficulty to use as two or more out of three. Major problems faced by patients using a pMDI included handling the device (27%) and hand-mouth co-ordination on device actuation (21%). Thirty-seven per cent stated that they had a problem with the pMDI but could not specify its exact nature. A spacer device had been prescribed for 76% of the MDI users in

this survey in order to counteract some of these problems, however, 85% of these patients did not utilise their spacer with their inhaler.

In terms of symptom relief achieved from inhaled bronchodilators, 31 of the 53 (58%) patients using a pMDI alone felt able to identify a 'clinical benefit' in comparison to 4 of the 12 (33%) DPI users. Although most DPI users (10/12) had rated their inhaler as easy to use, 50% were 'unsure' as to whether they received any benefit.

Relationship between disease severity and measured PIF at different resistances

In the patient group as a whole there was an inverse relationship between measured PIF and increased inhaler resistances. Furthermore there was stepwise decline in PIF rate with disease severity (Table 1).

The minimum required peak inspiratory flow (MRPIF) for adequate use of a pMDI is quoted as 25 l/min [13] and the mean [\pm SD] achieved by all patients was 98 [\pm 25] l/min (mild COPD: 107 \pm 20 l/min, moderate COPD: 78 \pm 22 l/min and severe COPD: 80 l/min) with the appropriate resistance setting for this device. By contrast, all patients achieved lower PIFs with the setting for the higher resistance DPI device (Turbohaler), which has been widely accepted as requiring a minimum PIF of 60 l/min according to the National Institute of Clinical Excellence (NICE) guidelines and the manufacturer [14]. The mean PIF for all patients at this resistance setting was 44 \pm 19 l/min (mild COPD: 54 \pm 15 l/min, moderate COPD: 27 \pm 6 l/min and severe COPD: 18 l/min). Furthermore, a significant correlation was noted between PIF at the highest resistance and disease severity (Figure 1).

Most patients were able to achieve the minimum PIF necessary for the other lower resistance devices but by only a relatively small margin in the moderate and severe COPD group. Of the seven patients who had been prescribed Turbohaler, only one was able to generate the minimal recommended PIF rate necessary for that device.

Relationship between PIF, age and disease severity

Assessment using stepwise multivariate linear regression showed that both age and COPD disease severity were independent variables influencing PIF. The estimated decrease in PIF between mild and severe disease patient groups was around 21 l/min, more than that seen between mild and moderate disease groups (approximately 13 l/min) for individuals of the same age ($P < 0.0001$). A significant negative correlation was found between age and the PIF rate achieved when assessed using the high resistance device setting ($R = 0.84$, $P < 0.0001$, refer Figure 2). The significant effect of age on PIF was independent of the disease grade and PIF can be estimated using the following:

Est PIF = 166.8 – 1.493 * age [years] (for mild disease), –13.14 (if moderate COPD) and –21.25 (if severe COPD).

Discussion

We have demonstrated that there are problems with the degree of satisfaction and practical usage of some of the inhalers prescribed to this elderly population. This is important since COPD is a disease of older age and optimum adherence to inhaler treatment may prevent acute exacerbations [15]. Our study was carried out in the 'real world' setting of general practice and included a wide spectrum of patients with a range of disease severity and age. The aim was to review the drug delivery devices actually used by these patients with COPD as well as the appropriateness of possible alternative devices in this elderly population.

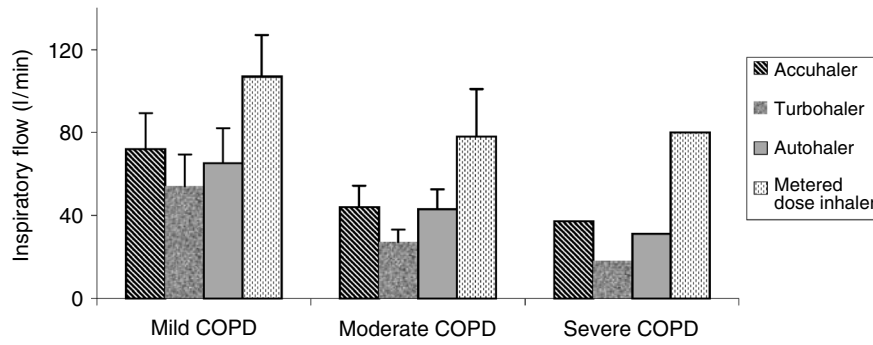
We based our questionnaire on previous studies, which have also looked at ease of inhaler use [16]. The ability to assess patient preference and satisfaction by means of a questionnaire has only been partially validated [17]. In our study, we chose to use a directed questionnaire approach as we thought that in our population of patients who may have difficulties this may be more appropriate. It also gave us the opportunity to be clear that a categorical answer was required. We found that 59% of the 53 patients using the pMDI identified problems with co-ordination and device handling, as noted previously [18]. Nevertheless, although 76% of the patients had a spacer available, 85% did not use it with their pMDI. The majority of DPI users (10/12 patients) reported < 2 on the difficulty rating scale in using their device. However, 6/12 of the patients were unsure if they received any benefit from their DPI. We chose to ask about perceived clinical benefit rather than attempt to determine actual measured benefit because this would be very difficult at a single visit; as by definition most patients with COPD have limited reversibility with a β_2 -agonist bronchodilator, although they may have improved walking distance [19].

The pMDI has previously been shown to be the most difficult inhaler device to use although the errors in technique were also noted with the Autohaler and Turbohaler [20]. We have found little published data on the use of pMDIs in an elderly COPD population. A large general practice base assessed 3,811 patients' 'real life' use of inhalers and the GPs ability to assess inhaler technique. Although only 25% of the patients were over 65, it highlighted similar problems with the pMDI, which was used incorrectly by 14–90% of adult patients [8] with as many as 89% of patients making at least one error [21].

Alternative devices particularly DPIs have been produced to overcome the problems with pMDIs. They tend to be more expensive, less complicated to manufacture and cater for some inhaled drugs, which are unstable in the pMDI form. However when a new device is assessed, it is invariably compared to the pMDI, the oldest and most established benchmark. Many such comparisons include only patients who correctly use the devices tested [22] and are not necessarily representative of the 'real-world'.

In our cohort of elderly patients with COPD, only 25% generated the minimum recommended PIF for the highest

Table 1. Inspiratory flow in elderly COPD patients according to different degrees of resistance



	Accuhaler* (l/min)	Turbohaler* (l/min)	Autohaler* (l/min)	pMDI* (l/min)
Mild	72 ± 17	54 ± 15	65 ± 16	107 ± 20
Moderate	44 ± 10	27 ± 6	43 ± 10	78 ± 22
Severe	37	18	31	80
All Patients	63 ± 20	44 ± 19	58 ± 18	98 ± 25

* Minimum required inspiratory flow rate: MDI, 25 l/min; Autohaler, 30 l/min; Accuhaler, 30 l/min; Turbohaler, 60 l/min

The relationship between FEV1 and peak inspiratory flow (PIF)

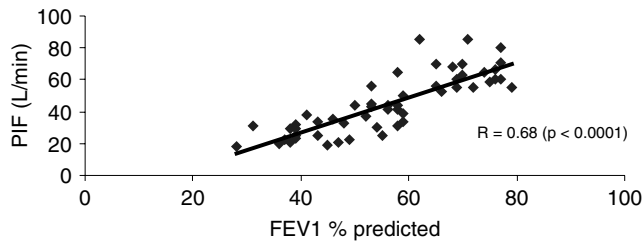


Figure 1.

Peak inspiratory flow (PIF) according to Age and Disease Severity

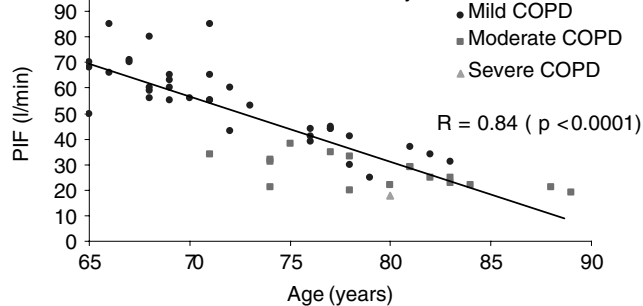


Figure 2.

resistance device. Sixty percent of patients with mild COPD and all patients with moderate COPD, respectively, failed to achieve an adequate PIF for the higher resistance device (overall mean PIF of <45 l/min) and those who could achieve an acceptable PIF for the lower resistance DPI or

improved pMDI, the Autohaler, often did so by only a small margin.

The minimum PIF required to operate a device effectively clearly influences clinical benefit. One group showed a reduction in drug deposition from 28% to 15%, when PIFs were reduced from 58 l/min to 36 l/min with drug deposition reduced as much as 50% when PIF decreased from 60 l/min to 30 l/min [21]. In our study even for the pMDI, the PIF decreased with increasing disease severity. In terms of the DPI, all of the seven patients prescribed a Turbohaler in the study rated it as easy to use. However, only one patient was able to achieve the NICE and manufacturer recommended minimum PIF of 60 l/min which accords with another study which showed that only 2 of 16 patients prescribed a Turbohaler had sufficient PIF required for optimum use of the device [23]. A recent study suggests a lower PIF requirement for Turbohaler [24]. There have been similar findings in children [25].

Therefore, even in a clinic setting, with the PIF measured by one investigator motivating patients to obtain the highest possible PIF values, the minimum PIF required for optimum inhaler use was barely achieved in many cases. It is therefore likely that at home, particularly patients during a disease exacerbation mild, moderate or severe COPD will not generate an adequate PIF. Since a number of patients with mild COPD may not meet specialist referral criteria [10] and be treated solely in the community, these findings have important implications for general practitioners.

The inability to produce an adequate PIF in our elderly population may be attributable to the disease. COPD reduces inspiratory muscle function due to lung hyperinflation. Muscle mass and fibre size are reduced and fibre type altered [26]. PIF is also reduced in chronic heart failure,

which often occurs as a co-morbidity in elderly patients [27]. In addition, there is a reduction in diaphragmatic strength by 25% in healthy elderly individuals compared to young adults [28]. Other physiological age-related changes e.g. kyphoscoliosis and arthritis of the costovertebral joints may affect the ability of the elderly patient to carry out the inspiratory manoeuvres required to get effective usage from some DPI devices.

Limitations of the study include the problem that there is no formal validated questionnaire assessing patient satisfaction and preference with inhalers and as this was a single visit study, repeatability was not tested. Additionally, since this was a prospective pilot study, in an area with little published data in the elderly [21], no prospective power calculation of sample size was possible. However, a retrospective power calculation showed our sample size was more than adequate (20 and 14 individuals would have 80%+ power to detect the effect of disease class and age respectively $P < 0.001$) on PIF and the results were significant to detect the independent effects of both COPD severity and age on PIF. Another limitation of the study may be that PIF should have been measured together with spirometry, but the In-Check Dial has been well validated [3, 11, 12, 22, 24] and in this context, is easy to use by both investigator and patient and would be a useful tool in the general practice setting.

It is important to consider that a number of drugs for COPD are not available in the entire range of different inhaler devices, which may limit choice when prescribing. For the use of a pMDI, spacers appear an obvious solution to many of the problems but are unpopular in practice. The ideal inhaler for all patients does not exist and the choice of device is particularly problematic in the elderly patient. Future development of new devices including cheap, portable, user-friendly, 'smart' nebulisers may be helpful for the elderly patient with COPD.

Key points

- Many patients are unhappy with their prescribed inhaler. Those who are satisfied with their inhaler are often unsure if they are receiving any clinical benefit.
- A large percentage of mild and moderate elderly patients with COPD are unable to generate adequate PIFs for the optimum use of some popular DPI devices.
- Many (85%) patients who were prescribed a large volume spacer did not use it.
- The relationship between poor inspiratory flow and age is multifactorial. Factors include the effects of ageing, COPD severity, nutrition and co-morbidities.

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Conflicts of Interest

None declared.

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