A Clinical Tool to Assess Inhalation Profiles in Patients Affected by Lung Diseases: Preliminary Results

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Abstract

It has been reported that asthmatic and COPD (chronic obstructive pulmonary diseases) patients struggle to use their inhalers correctly. Studies have shown after training the flow rates achieved by patients can be compromised due to the high resistance of their prescribed inhaler. The aim of this work was to provide preliminary data on the future applicability of a diagnostic tool to guide DPI (dry powder inhaler) choice based on inhalation profiles achieved by patients. Inhalation profiles were recorded using a variable resistance device in series with a conventional clinical spirometer for 20 severe asthmatic and 20 COPD patients. The severity of the disease was assessed following GINA guidelines. The patients were asked to inhale as they would when taking their medication. Descriptive metrics were extracted using a computational curve-stripping approach and preliminary analysis is reported here for peak inspiratory flow (PIF). There was no significant difference between groups for a specific inhaler resistance (e.g. 82.51 ± 28.64 Lmin\(^{-1}\) for 0.158 cmH\(_2\)O resistance in COPD patients and 77.89 ± 28.05 Lmin\(^{-1}\) in severe asthmatics, p < 0.05). However, the study showed that patients without training achieved flow rates (>100 Lmin\(^{-1}\)) when inhaling against low resistance (representing a metered dose inhaler). On the other hand, patients inhaled for longer when a high resistance device was simulated than for a low resistance device. Other parameters such as acceleration of the flow and time of inhalation will be taken into account to use the full inhalation profiles for routine clinical guide for inhaler choice.

Introduction:

Recent studies [1, 2] have shown patients having difficulties in using the appropriate technique through their devices. The majority of the patients is not aware of the difference techniques in using MDIs (metered dose inhalers) or DPI (dry powder inhalers), resulting in a lower dose delivered to the lungs [1]. For an MDI a slow and deep manoeuvre is needed when inhaling the formulation, whilst for the DPIs, a fast and deep inhalation is required in order to create turbulent energy for aerosolization of the dose [2]. Some studies [3, 4] have focused their aims on studying the peak inspiratory flow (PIF) of a group of COPD (chronic obstructive pulmonary disease) patients through particular devices. One study suggested that some patients can inhale correctly through the device provided [4] (e.g. Turbuhaler for COPD patients) and another suggested that, especially in elderly patients, the flow rate achievable could be compromised probably due to the high resistance of the inhaler prescribed [3].

A few research groups [5, 6] have focused their work on creating or collecting inhalation profiles for in vitro testing of inhalers. Therefore, the inhalation manoeuvre is important to consider when choosing the appropriate device. Some studies in the US and in the EU have been completed [7, 8] on collection of inhalation profiles through specific devices. The authors used a pneumotrac spirometer attached to marketed devices and measured the inhalation profile using the inhalation manager (i.e. a computer-controlled flow-volume simulator). Although their methods gave interesting information regarding the inhalation profiles, it required multiple inhalers with placebo or medicine. Sometimes a propellant might be involved that can increase the risk of having aerosol impacting on the patient’s throat.

The aim of this work was to provide preliminary data on the future applicability of a diagnostic tool to guide DPI choice based on inhalation profiles achieved by patients. In this abstract, only the PIF and IV (inhaled volume) parameters will be assessed to identify the utility of the tool. However, more metrics will be taken into account in future work, with the intention of identifying the effect of inhaler resistance on the full inhalation profile of a wide range of patients affected either by mild, moderate, severe asthma or COPD. In contrast to previous studies, in the current work neither placebo nor propellant was used. Three devices (MDI, Aerolizer and Handihaler that represent ultralow resistance, low and high resistance devices, respectively) were tested with 40 patients (20 severe asthmatics and 20 COPD patients). The severity of the disease was assessed following GINA guidelines.
Methods:

An ethical and R&D approval (REC number: 13/LO/0970 and Study ID: 122645) was obtained through the Royal Brompton Hospital (London) in order to recruit 20 severe asthmatics and 20 COPD patients and to perform lung function and inhalation profile collection through a devices with variable resistance to airflow. All patients completed a full lung function test as part of the protocol. The participants then inhaled through the a Pneumotrac (MasterScreen™ Pneumo Spirometer, CareFusion, Basingstoke, UK) attached to a mouthpiece containing a rotating disk (Clement Clarke International Ltd., Harlow, UK) containing different holes with variable diameters. The holes represent the resistances of marketed inhalers (e.g. MDI, Aerolizer (Novartis Pharma AG) and Handihaler (Boehringer Ingelheim GmbH & Co. Figure 1). The patients were asked to inhale as they would when taking their medication.

![Image](image.png)

Figure 1. Inhalation profile measurements set up.

Participants were permitted to practice an inhalation manoeuvre under training prior to the recorded inhalation. The profiles were then recorded and the PIF and IV statistically analysed in OriginLab software.

Results and discussion:

The full lung function testing (FEV<sub>1</sub>, forced expiratory volume in 1 s, FVC, forced vital capacity and the ratio of the two values) are reported in Table 1.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>COPD</th>
<th>Severe asthma</th>
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<tbody>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; (% pred)</td>
<td>54.79 ± 26.61</td>
<td>63.21 ± 27.09</td>
</tr>
<tr>
<td>FVC (% pred)</td>
<td>87.79 ± 27.87</td>
<td>80.89 ± 24.27</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;/FVC (%)</td>
<td>62.13 ± 18.19</td>
<td>77.52 ± 23.51</td>
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In Figure 2 (A, B) a representative inhalation profiles for each ‘device’ resistance is presented for the two groups of patients.

![Figure 2](image.png)

Figure 2. Representative inhalation profiles against time through resistance simulating an MDI (blue), the Aerolizer (red) and the Handihaler (green) devices for COPD patients (A) and severe asthmatic patients (B).
The majority of the patients demonstrated inappropriate technique when inhaling through the MDI as shown in Figure 2 (red line). The rapid manoeuvre was achieved owing to the poor perception of flow rate against the low resistance. The MDI is an ultralow-resistance device, which means that it is relatively easy to generate too great an inspiratory flow, which is a common error in the use of MDIs [2]. On the other hand, when testing the Handihaler (resistance 0.158 cmH₂O), a lower profile plateau was observed (Figure 2, A). As previously reported [9], the patients showed a prolonged breath profile when the highest resistance device (i.e. Handihaler) was tested (Figure 2). In Table 2, the mean of the PIF and IV achieved by the patients are reported.

Table 2. Values of peak inspiratory flow (PIF) and inhaled volume (IV) measured for two groups of patients through three inhalers (mean ± SD, n=20)

<table>
<thead>
<tr>
<th>Groups</th>
<th>PIF (L/min)</th>
<th>IV (l)</th>
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<tr>
<td></td>
<td>COPD MDI</td>
<td>COPD Aerolizer</td>
</tr>
<tr>
<td>COPD</td>
<td>133.33 ± 43.30</td>
<td>147.57 ± 43.71</td>
</tr>
<tr>
<td>Severe asthmatics</td>
<td>141.72 ± 53.21</td>
<td>133.44 ± 41.19</td>
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</table>

The PIFs achieved for the MDI were higher the previously reported data for patients with good technique [10], although patients with poor technique do inhale as rapidly as 240 L/min⁻¹ [11]. However, for within disease group comparisons, patients inhaling through the Aerolizer, achieved a greater PIF and IV than following inhalation through the Handihaler (paired t-test, p<0.05, Table 2). No significant difference was seen when a given inhaler was compared between asthmatics and COPD patients (unpaired t-test, p>0.05, Figure 3). A similar trend of higher IV for a low resistance devices was observed. Unlike the PIF, a significant difference was seen for IV between disease groups for the Aerolizer and the Handihaler (unpaired t-test, p<0.05, Table 2).

Figure 3. Statistical analysis of PIF (peak inspiratory flow) on MDI (A), Aerolizer (B) and Handihaler (C) between groups of patients (mean ± SD, n=20).

Conclusions

The study showed no significant difference in one metric of inhalation performance (the peak inspiratory flow) between patient disease groups when examining specific inhalation device resistances, although within groups, patients achieved low flow rates for a device with high (0.158 cmH₂O) resistance to airflow (i.e. Handihaler) than a device with 0.05 cmH₂O resistance to the air (Aerolizer). Significant difference was seen in the IV, instead, suggesting the using only the PIF as a solely metric is not appropriate. Other parameters, such as acceleration of the flow and inhalation time, will be taken into account to fully understand the inhalation profiles achievable against a representative range of pressure drops. Moreover, the parameters will be used in vitro using a Breath Simulator to fully understand the pharmaceutical performance of the medication when a specific inhaler is used. This project has shown preliminary data for development of a spirometry tool, which following incorporation of
future work on aerodynamic performance assessment could be used for rapid clinical identification of DPI suitability for patients. This tool could be transferable to other devices that possess similar resistance during new product development.

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References