Peak inspiratory flow rate measurement by using In-Check DIAL for the different inhaler devices in elderly with obstructive airway diseases

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Background: Inhaler device technique is a common cause of treatment failure in patients with asthma and chronic obstructive pulmonary disease. Dry powder inhaler (DPI) requires optimal peak inspiratory flow rate (PIFR) for drug delivery. Low PIFR generation is common in the elderly. Patient lung function and intrinsic inhaler resistance are factors for determining generated PIFR and drug delivery from DPI.

Objectives: We aimed to identify the PIFR of the older (aged >60 years) and the younger (aged ≤60 years) patients with obstructive airway diseases for the different inhaler devices (Turbuhaler® and Accuhaler).

Patients and methods: A cross-sectional study was conducted from January to December 2014. Patients with obstructive airway diseases were recruited. Spirometry was performed. PIFR was measured by using an In-Check DIAL device. Individual PIFR values for each inhaler device were obtained for three consecutive measurements and then averaged.

Results: A total of 139 patients diagnosed with obstructive lung diseases (asthma, n = 109; chronic obstructive pulmonary disease, n = 30) were recruited. Of these, 71 patients (51%) were >60 years. The PIFR generated by the patients who were ≤60 years for nonresistance mode was not different from that generated by those aged >60 years (115.0 ± 15.2 L/min vs 115.4 ± 13.3 L/min, p = 0.86). Regarding the DPI, PIFR generated from the older group was significantly lower than that generated from the younger group for Turbuhaler (72.5 ± 18.8 L/min vs 82.4 ± 21.1 L/min, p = 0.01), but the PIFR generated was not significantly different between the older and the younger groups for the Accuhaler (93.8 ± 22.9 L/min vs 99.4 ± 24.2 L/min, p = 0.86). The low peak expiratory flow rate and PIFR from spirometry were associated with the suboptimal PIFR measured by using In-Check DIAL.

Discussion: Optimal PIFR is critical for DPI use in the elderly; appropriate DPI selection is essential for management. In-Check DIAL may be useful for detecting inhaler device problem among the elderly.

Conclusion: Lower PIFR generated from Turbuhaler was noted in patients with airway diseases who were older than 60 years, when compared to the younger patients.

Keywords: elderly, obstructive airway diseases, peak inspiratory flow rate, dry powder inhaler

Introduction
Inhaled therapies are the cornerstone for treatments of asthma and chronic obstructive pulmonary disease (COPD). Inhaled drugs provide better pulmonary bioavailability, lower dose requirement and less systemic toxicities than the oral or injectable drugs. However, deposition of inhaled drugs in the lungs is critically influenced by both inhaled drug delivery system and dose mixing system. Patient inhaler techniques and
fine particle fraction (FPF) must be taken into account for improving the distal lung deposition. For pressurized meter

dose inhaler (pMDI) device, manual dexterity and hand–lung

coordination are crucial. In contrast, generation of peak

inspiratory flow rate (PIFR) is an essential component for

use of dry powder inhaler (DPI). Optimal PIFR exerts an

effect on deagglomeration between active drugs and sugar

carriers. For this reason, ineffective PIFR generation in DPI

users is associated with less drug delivery to the distal lungs,

lower efficacy and poor clinical outcome. For this reason, ineffective PIFR generation in DPI

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Intrinsic resistance of the devices and inspiratory effort

of the patients are associated with the generated PIFR. A

previous study in COPD has shown that older COPD patients

are not able to generate optimal PIFR for DPI (>60 L/min).

However, there were no differences in PIFR for the DPI

comparing between elderly COPD patients and age-matched

elderly controls. Age rather than severity of airflow limitation

affects measured PIFR for DPI use. The generated PIFR of

older COPD does not reach the recommended PIFR, particu-

larly PIFR that is measured from Turbuhaler. These find-

ings reflect the controversial effect of intrinsic resistance of

different DPIs and aging on the PIFR generation. In-Check

DIAL device was developed to objectively assess PIFR. By

using this device, the optimal PIFR for DPI is 60 L/min. How-

ever, the use of In-Check DIAL is limited due to a lack

of familiarity and availability to general practitioners. In

addition, the clinical and physiological parameters such as

patient’s lung functions, forced expiratory volume in 1 second

(peak expiratory flow rate (PEFR) have never

been studied as predictors for the optimal PIFR generation

measured by using In-Check DIAL. We hypothesized that

the disease severity as determined by airflow obstruction and

aging affect the PIFR generation. Therefore, we conducted

this study to measure the PIFR in older (aged >60 years) and

younger (aged ≤60 years) patients with obstructive airway

diseases for the different inhaler devices. We also determined

whether the spirometric parameters were the predictors for

optimal PIFR generated by In-Check DIAL.

Patients and methods

We enrolled consecutive patients with obstructive airway dis-

eases (asthma and COPD), who were treated in the pulmonary

clinic, Ramathibodi Hospital, Mahidol University, Thailand,

from January to December 2014. The eligible patients for

this study were those who were able to perform spirometry

with acceptable and reproducible criteria according to the

American Thoracic Society and European Respiratory Soci-

ey standardization, and were able to correctly perform PIFR

measurement using In-Check DIAL following the instruction.

Ethical approval was obtained from the Committee on Human

Rights Related to Research Involving Human Subjects of

Ramathibodi Hospital, Mahidol University (ID 07-57-01). All

participants gave written informed consent.

Patient definition

Patients with asthma were clinically diagnosed according

to the Global Initiative for Asthma (GINA) 2014. Patients

with COPD were clinically diagnosed according to the Global

Initiative for Obstructive Lung Disease (GOLD) 2014.

Measurement

Spirometry was conducted by a certified technician (SK), and

the reference equation for normality was chosen according

to age, height, gender and race. Spirometry was performed

during the stable phase of the disease. Bronchodilator revers-

ibility testing was performed 15 minutes following adminis-

tration of 400 µg of salbutamol via spacer. The measurements

of PIFR for the different inhaler devices were performed by

SK using In-Check DIAL (Clement Clarke International,

Harlow, UK) as previously described. A total of three con-

secutive measurements of PIFR for each device (nonresistant mode, Accuhaler and Turbuhaler)

were performed following the instruction of measurement

previously published. The average values of PIFR from three

consecutive measurements were reported. The sequence of

measuring PIFR by In-Check DIAL was started with non-

resistant mode, Accuhaler and Turbuhaler, respectively.

Statistical analysis

The differences in the continuous variables of the two groups

of subjects aged >60 years and ≤60 years were tested by

using independent t-test. The differences in the continuous

variables among the three different devices were tested by

one-way analysis of variance. The predictors for subopti-

mальным PIFR (<60 L/min) for each device were determined

by logistic regression. Statistical significance was set at a

p-value of <0.05.

Results

A total of 139 patients with obstructive lung diseases were

recruited during the study period. The mean (SD) age was

59.5 (15.6) years. Of these, 71 patients (51%) were older

than 60 years. Asthma was diagnosed in 48.9% and COPD

in 51.1% of patients. The demographic and spirometric

parameters are listed in Table 1. The patients aged >60 years had a significantly lower pre-bronchodilator (pre-BD)
For the Accuhaler, 10 patients (9.3%) were unable to generate suboptimal PIFR due to the low PEFR <300 L/min and low PIFR <250 L/min. We found that the predictors of suboptimal PIFR during Turbuhaler use were pre-BD PEFR and post-BD PEFR <300 L/min, and pre-BD and post-BD PIFR <250 L/min (Table 3).

**Discussion**

The present study is a real-life study demonstrating that there was a significant lower PIFR generated from Turbuhaler in patients with obstructive lung diseases who were older than 60 years when compared to the younger patients.

Inhaler device misuse is commonly seen in the elderly and contributes to poor disease outcome or reduced disease control. 

Association between inhaler misuse and older age and lack of health caregiver instruction was noted in asthma and COPD. According to GINA recommendation, the selection of an appropriate device for the patients is a major consideration for prescribing inhaled medications.

The low inspiratory effort is a common inhaler problem in elderly using DPI. Technically, the PIFR can be assessed by using In-Check DIAL in both adults and children. A previous study conducted in older COPD and age-matched healthy subjects has shown that the ability to generate sufficient PIFR across different DPIs is impaired regardless of the presence of COPD. In addition, patients with suboptimal PIFR are varied in the elderly with airway diseases who used Turbuhaler. We found that one-fifth of patients could not generate optimal PIFR for Turbuhaler in our study, and the PIFR generated by the elderly for Turbuhaler was significantly lower compared to that generated by the younger patients. However, the PIFR generated by the elderly for Accuhaler was not significantly lower than that generated by the younger patients. These findings were analogous with the previous studies in which the lower PIFR was common in Turbuhaler and PIFR decreased significantly with age in Turbuhaler compared to Diskus.

The mechanism for the lower PIFR generated by different DPI types in the elderly is due to the different intrinsic device resistance and respiratory muscle function in aging. Since the intrinsic resistance of Turbuhaler is higher than that of Accuhaler, this could affect the PIFR generation and drug delivery performance while using the Turbuhaler in the elderly. The suboptimal PIFR generation during Turbuhaler use could be predicted by having the low PEFR <300 L/min and low PIFR <250 L/min but could not be predicted by having FEV1 <50% predicted from spirometry. Nonetheless, these parameters did not influence the PIFR generation while using an Accuhaler.

**Table 1** Demographic and spirometric parameters of the patients with obstructive lung diseases (age >60 years vs age ≤60 years)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Age &gt;60 years (n = 71)</th>
<th>Age ≤60 years (n = 68)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male), n (%)</td>
<td>54 (79.4)</td>
<td>14 (20.6)</td>
<td>0.007</td>
</tr>
<tr>
<td>Diagnosis, n (%)</td>
<td></td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>Asthma</td>
<td>48 (67.6)</td>
<td>61 (89.7)</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>23 (32.4)</td>
<td>7 (10.3)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>62.3 ± 12.1</td>
<td>62.6 ± 11.9</td>
<td>0.890</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158.1 ± 7.9</td>
<td>158.3 ± 7.9</td>
<td>0.882</td>
</tr>
<tr>
<td>Pre-BD FEV1 (%)</td>
<td>72.6 ± 20.9</td>
<td>77.9 ± 18.1</td>
<td>0.116</td>
</tr>
<tr>
<td>Post-BD FEV1 (%)</td>
<td>76.9 ± 20.3</td>
<td>81.2 ± 18.2</td>
<td>0.195</td>
</tr>
<tr>
<td>Pre-BD FEV1/FVC (%)</td>
<td>64.3 ± 12.8</td>
<td>72.9 ± 11.6</td>
<td>0.00*</td>
</tr>
<tr>
<td>Post-BD FEV1/FVC (%)</td>
<td>66.2 ± 12.3</td>
<td>75.8 ± 11.9</td>
<td>0.00*</td>
</tr>
<tr>
<td>Pre-BD PEFR (L/min)</td>
<td>298.1 ± 111.2</td>
<td>361.1 ± 95.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Post-BD PEFR (L/min)</td>
<td>307.2 ± 110.6</td>
<td>375.4 ± 91.9</td>
<td>0.00*</td>
</tr>
<tr>
<td>Pre-BD PIFR (L/min)</td>
<td>225.4 ± 86.8</td>
<td>274.1 ± 91.7</td>
<td>0.002</td>
</tr>
<tr>
<td>Post-BD PIFR (L/min)</td>
<td>226.2 ± 88.3</td>
<td>284.0 ± 88.7</td>
<td>0.00*</td>
</tr>
</tbody>
</table>

**Notes:** Data are presented as n (%) and mean ± SD. *p < 0.001.

**Abbreviations:** COPD, chronic obstructive pulmonary disease; pre-BD, pre-bronchodilator; FEV1, forced expiratory volume in 1 second; post-BD, post-bronchodilator; FVC, forced vital capacity; PEFR, peak expiratory flow rate; PIFR, peak inspiratory flow rate; SD, standard deviation.
Table 2 Spirometric parameters and PIFR measured by using In-Check DIAL device for the patients with obstructive lung diseases (age >60 years vs age ≤60 years) stratified by type of inhaler devices

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Age &gt;60 years</th>
<th>Turbuhaler (n = 62)</th>
<th>Accuhaler (n = 60)</th>
<th>Age ≤60 years</th>
<th>Turbuhaler (n = 47)</th>
<th>Accuhaler (n = 47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-BD FEV₁ (% predicted)</td>
<td>72.0 ± 21.7</td>
<td>72.7 ± 21.2</td>
<td>72.2 ± 21.4</td>
<td>77.9 ± 18.4</td>
<td>76.3 ± 17.5</td>
<td>75.5 ± 16.9</td>
</tr>
<tr>
<td>Pre-BD PEF/L (min)</td>
<td>298.1 ± 112.9</td>
<td>298.4 ± 114.1</td>
<td>301.7 ± 111.9</td>
<td>361.5 ± 96.2</td>
<td>362.3 ± 101.9</td>
<td>360.8 ± 101.0</td>
</tr>
<tr>
<td>Pre-BD PIFR (L/min)</td>
<td>220.7 ± 86.5</td>
<td>225.9 ± 86.2</td>
<td>229.2 ± 90.7</td>
<td>274.4 ± 94.4</td>
<td>283.3 ± 91.4</td>
<td>275.4 ± 98.9</td>
</tr>
<tr>
<td>Post-BD FEV₁ (% predicted)</td>
<td>76.4 ± 21.1</td>
<td>77.0 ± 20.6</td>
<td>76.1 ± 20.8</td>
<td>80.8 ± 17.9</td>
<td>79.9 ± 18.6</td>
<td>78.8 ± 17.1</td>
</tr>
<tr>
<td>Post-BD PIFR (L/min)</td>
<td>220.7 ± 83.6</td>
<td>224.4 ± 84.7</td>
<td>228.7 ± 92.7</td>
<td>283.2 ± 91.7</td>
<td>289.0 ± 88.5</td>
<td>282.8 ± 94.6</td>
</tr>
<tr>
<td>PIFR from In-Check DIAL (L/min)</td>
<td>115.4 ± 13.3</td>
<td>72.5 ± 18.9</td>
<td>93.8 ± 22.9</td>
<td>115.0 ± 15.2</td>
<td>82.5 ± 21.1</td>
<td>99.5 ± 24.3</td>
</tr>
</tbody>
</table>

Notes: Data are presented as mean ± SD. *p < 0.01.
Abbreviations: PIFR, peak inspiratory flow rate; pre-BD, pre-bronchodilator; FEV₁, forced expiratory volume in 1 second; PEF, peak expiratory flow rate; post-BD, post-bronchodilator; SD, standard deviation.

Table 3 Pre-BD and post-BD spirometric parameters and the associations with suboptimal PIFR (<60 L/min) measured by In-Check DIAL for Turbuhaler and Accuhaler

<table>
<thead>
<tr>
<th>Spirometric variables</th>
<th>Odds ratio for having suboptimal PIFR (&lt;60 L/min)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turbuhaler</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-BD FEV₁ &lt;50% predicted</td>
<td>0.93</td>
<td>0.22–3.89</td>
</tr>
<tr>
<td>Post-BD FEV₁ &lt;50% predicted</td>
<td>1.32</td>
<td>0.29–5.88</td>
</tr>
<tr>
<td>Pre-BD PEF &lt;300 L/min</td>
<td>1.98</td>
<td>1.40–2.80</td>
</tr>
<tr>
<td>Post-BD PEF &lt;300 L/min</td>
<td>2.00</td>
<td>1.31–3.05</td>
</tr>
<tr>
<td>Pre-BD PIFR &lt;250 L/min</td>
<td>1.76</td>
<td>1.31–2.36</td>
</tr>
<tr>
<td>Post-BD PIFR &lt;250 L/min</td>
<td>1.72</td>
<td>1.27–2.33</td>
</tr>
<tr>
<td>Accuhaler</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-BD FEV₁ &lt;50% predicted</td>
<td>1.92</td>
<td>0.48–7.56</td>
</tr>
<tr>
<td>Post-BD FEV₁ &lt;50% predicted</td>
<td>2.40</td>
<td>0.58–9.79</td>
</tr>
<tr>
<td>Pre-BD PEF &lt;300 L/min</td>
<td>1.68</td>
<td>1.05–2.68</td>
</tr>
<tr>
<td>Post-BD PEF &lt;300 L/min</td>
<td>1.69</td>
<td>0.95–3.00</td>
</tr>
<tr>
<td>Pre-BD PIFR &lt;250 L/min</td>
<td>1.50</td>
<td>1.04–2.16</td>
</tr>
<tr>
<td>Post-BD PIFR &lt;250 L/min</td>
<td>1.46</td>
<td>1.02–2.09</td>
</tr>
</tbody>
</table>

Abbreviations: pre-BD, pre-bronchodilator; post-BD, post-bronchodilator; PIFR, peak inspiratory flow rate; FEV₁, forced expiratory volume in 1 second; PEF, peak expiratory flow rate; CI, confidence interval.

Since DPI is popular among inhaled devices in respiratory medicine including asthma and COPD,17–26 the low PIFR tended to be associated with poor asthma control among the Turbuhaler users compared to Accuhaler users was noted in asthma treated with inhaled corticosteroid delivered by DPI.6 Caution should be taken in the older asthmatics with severe airway obstruction and suboptimal PIFR who use DPI.16 However, disease-specific clinical outcome was not measured in our study, despite the ability to identify asthma and COPD patients with inadequate PIFR providing potential interventions.27 In the lack of availability of In-Check DIAL device in routine clinical practice, there has been a role of spirometry for predicting suboptimal PIFR measured by In-Check DIAL.

We acknowledged that our study had some limitations. First, the measurement of PIFR using In-Check DIAL was performed after a variable period of bronchodilator administration, which could affect the performance of power for PIFR generation. Second, the age threshold was chosen as 60 years in our study, while clinical studies were conducted in elderly with a chronological age of ≥65 years,28 since older people are defined by the age of ≥60 years. Recently, the definition of an elderly person in Thailand has been updated, based on the 2014 Survey of Older Population, into a universal social pension for Thai people aged ≥60 years.29 In addition, the World Health Organization defines older people as those aged 60 years for developing countries and 65 years for developed countries.30

**Conclusion**
Lower peak inspiratory flow generated during Turbuhaler was noted in patients with obstructive lung diseases who were older than 60 years, compared to the younger patients. No difference in PIFR generation from Accuhaler was observed between them. The suboptimal PIFR measured by In-Check DIAL was predicted by low PIFR and PEF from spirometry.

**Disclosure**
The authors report no conflicts of interest in this work.

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27. Melani AS, Bracci LS, Rossi M. Reduced peak inspiratory effort through Diskus® and Turbuhaler® inhalers (Diskus® and Turbuhaler®) and relationships with asthma control. Int J Chron Obstruct Pulmon Dis. 2010;5:257–262.

