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ORIGINAL RESEARCH

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

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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.[1] However, deposition of inhaled drugs in the lungs is critically influenced by both inhaled drug delivery system and dose mixing system.[2] Patient inhaler techniques and fine particle fraction (FPF) must be taken into account for improving the distal lung deposition.[3] For pressurized meter dose inhaler (pMDI) device, manual dexterity and hand–lung coordination are crucial.[4] In contrast, generation of peak inspiratory flow rate (PIFR) is an essential component for usage of dry powder inhaler (DPI).[4] 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.[5,6]

Intrinsic resistance of the devices and inspiratory effort of the patients are associated with the generated PIFR.[7] 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.[8] Age rather than severity of airflow limitation affects measured PIFR for DPI use.[9] The generated PIFR of older COPD does not reach the recommended PIFR, particularly PIFR that is measured from Turbuhaler®. These findings reflect the controversial effect of intrinsic resistance of different DPIs and aging on the PIFR generation.[7] In-Check DIAL device was developed to objectively assess PIFR.[10,11] By using this device, the optimal PIFR for DPI is 60 L/min.[8] However, 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 (FEV_1) and 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 diseases (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 Society standardization,[12] 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.[13] Patients with COPD were clinically diagnosed according to the Global Initiative for Obstructive Lung Disease (GOLD) 2014.[14]

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 reversibility testing was performed 15 minutes following administration 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.[15]

A total of three consecutive measurements of PIFR for each device (nonresistant mode, Accuhaler and Turbuhaler) were performed following the instruction of measurement previously published.[8] The average values of PIFR from three consecutive measurements were reported. The sequence of measuring PIFR by In-Check DIAL was started with nonresistant 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 suboptimal 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)

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

Variables	Age >60 years (n = 71)	Age ≤60 years (n = 68)	*p*-value
Gender (male), n (%)	54 (79.4)	14 (20.6)	0.007
Diagnosis, n (%)			0.002
Asthma	48 (67.6)	61 (89.7)	
COPD	23 (32.4)	7 (10.3)	
Weight (kg)	62.3 ± 12.1	62.6 ± 11.9	0.890
Height (cm)	158.1 ± 7.9	158.3 ± 7.9	0.882
Pre-BD FEV_1 (% predicted)	72.6 ± 20.9	77.9 ± 18.1	0.116
Post-BD FEV_1 (% predicted)	76.9 ± 20.3	81.2 ± 18.2	0.195
Pre-BD FEV_1/FVC (%)	64.3 ± 12.8	72.9 ± 11.6	0.00*
Post-BD FEV_1/FVC (%)	66.2 ± 12.3	75.8 ± 11.9	0.00*
Pre-BD PEFR (L/min)	298.1 ± 111.2	361.1 ± 95.0	0.001
Post-BD PEFR (L/min)	307.2 ± 110.6	375.4 ± 91.9	0.00*
Pre-BD PIFR (L/min)	225.4 ± 86.8	274.1 ± 91.7	0.002
Post-BD PIFR (L/min)	226.2 ± 88.3	284.0 ± 88.7	0.00*

Notes: Data are presented as n (%) and mean ± SD. *$p < 0.001$.
Abbreviations: COPD, chronic obstructive pulmonary disease; pre-BD, pre-bronchodilator; FEV_1, 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.

FEV_1/forced vital capacity (FVC) and post-bronchodilator (post-BD) FEV_1/FVC, pre-BD PEFR and post-BD PEFR (L/min) and pre-BD PIFR and post-BD PIFR (L/min) than those aged <60 years. Regarding the type of inhaler devices, although there were no differences in the severity of airflow obstruction reflected by pre-BD and post-BD FEV_1 among the three inhaler devices, there were significantly less pre-BD PIFR and post-BD PIFR generated during spirometry as well as less pre-BD PEFR and post-BD PEFR in those aged >60 years in the Turbuhaler and Accuhaler groups (Table 2).

There were no differences in PIFR measured by In-Check DIAL for the nonresistant mode and Accuhaler between patients aged >60 years and ≤60 years (115.4 ± 13.3 L/ min vs 115 ± 15.2 L/min, $p = 0.86$, and 93.8 ± 22.9 L/min vs 99.4 ± 24.3 L/min, $p = 0.22$, respectively). However, lower PIFR for the Turbuhaler was noted in the older patients when compared to the younger patients (72.5 ± 18.9 L/min vs 82.5 ± 21.1 L/ min, $p = 0.01$; Table 2).

Of the 109 patients in whom PIFR was measured for Turbuhaler, 21 patients (19.3%) generated suboptimal PIFR measured by In-Check DIAL <60 L/min (mean PIFR In-Check DIAL: 46.64 ± 7.8 L/min vs 84.0 ± 15.1 L/min). Whereas, of the 107 patients in whom PIFR was measured for Accuhaler, 10 patients (9.3%) were unable to generate effective PIFR >60 L/min (mean PIFR In-Check DIAL: 48.4 ± 9.2 L/min vs 101.2 ± 18.5 L/min, $p = 0.71$). The spirometric parameters or factors were analyzed for their association with lower PIFR for Turbuhaler. 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.[16,17] Association between inhaler misuse and older age and lack of health caregiver instruction was noted in asthma and COPD.[18] According to GINA recommendation, the selection of an appropriate device for the patients is a major consideration for prescribing inhaled medications.[13] The low inspiratory effort is a common inhaler problem in elderly using DPI.[4] Technically, the PIFR can be assessed by using In-Check DIAL in both adults and children.[8,10,19] 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.[8] In addition, patients with suboptimal PIFR are varied in the elderly with airway diseases who used Turbuhaler.[20,21] 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®.[6,15,22] 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[23] Since the intrinsic resistance of Turbuhaler is higher than that of Accuhaler,[24] this could affect the PIFR generation and drug delivery performance while using the Turbuhaler in the elderly.[7,25] 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 FEV_1 <50% predicted from spirometry. Nonetheless, these parameters did not influence the PIFR generation while using an Accuhaler.

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

Parameters	Age >60 years			Age ≤60 years		
	Nonresistant mode (n = 64)	Turbuhaler (n = 62)	Accuhaler (n = 60)	Nonresistant mode (n = 62)	Turbuhaler (n = 47)	Accuhaler (n = 47)
Pre-BD FEV_1 (% predicted)	72.0 ± 21.7	72.7 ± 21.2	72.2 ± 21.4	77.9 ± 18.4	76.3 ± 17.5	75.5 ± 16.9
Pre-BD PEFR (L/min)	298.1 ± 112.9	298.4 ± 114.1*	301.7 ± 111.9*	361.5 ± 96.2	362.3 ± 101.9	360.8 ± 101.0
Pre-BD PIFR (L/min)	220.7 ± 86.5*	225.9 ± 86.2*	229.2 ± 90.7*	274.4 ± 94.4	283.3 ± 91.4	275.4 ± 98.9
Post-BD FEV_1 (% predicted)	76.4 ± 21.1	77.0 ± 20.6	76.1 ± 20.8	80.8 ± 17.9	79.9 ± 18.6	78.8 ± 17.1
Post-BD PIFR (L/min)	220.7 ± 83.6	224.4 ± 84.7*	228.7 ± 92.7*	283.2 ± 91.7	289.0 ± 88.5	282.8 ± 94.6
PIFR from In-Check DIAL (L/min)	115.4 ± 13.3	72.5 ± 18.9*	93.8 ± 22.9	115.0 ± 15.2	82.5 ± 21.1	99.5 ± 24.3

Notes: Data are presented as mean ± SD. *$p < 0.01$.
Abbreviations: PIFR, peak inspiratory flow rate; pre-BD, pre-bronchodilator; FEV_1, forced expiratory volume in 1 second; PEFR, 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

Spirometric variables	Odds ratio for having suboptimal PIFR (<60 L/min)	95% CI
Turbuhaler		
Pre-BD FEV_1 <50% predicted	0.93	0.22–3.89
Post-BD FEV_1 <50% predicted	1.32	0.29–5.88
Pre-BD PEFR <300 L/min	1.98	1.40–2.80
Post-BD PEFR <300 L/min	2.00	1.31–3.05
Pre-BD PIFR <250 L/min	1.76	1.31–2.36
Post-BD PIFR <250 L/min	1.72	1.27–2.33
Accuhaler		
Pre-BD FEV_1 <50% predicted	1.92	0.48–7.56
Post-BD FEV_1 <50% predicted	2.40	0.58–9.79
Pre-BD PEFR <300 L/min	1.68	1.05–2.68
Post-BD PEFR <300 L/min	1.69	0.95–3.00
Pre-BD PIFR <250 L/min	1.50	1.04–2.16
Post-BD PIFR <250 L/min	1.46	1.02–2.09

Abbreviations: pre-BD, pre-bronchodilator; post-BD, post-bronchodilator; PIFR, peak inspiratory flow rate; FEV_1, forced expiratory volume in 1 second; PEFR, 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 PEFR from spirometry.

Disclosure

The authors report no conflicts of interest in this work.

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