

Impact of exacerbation on the errors of inhaler techniques in COPD patients

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ABSTRACT

Identification of poor inhaler technique is vital for COPD management at time of hospital discharge and thereafter. This observational study aimed to determine the impact of exacerbation on the errors of inhaler techniques among COPD patients. The study was conducted in chest clinic at Central Chest Institute of Thailand. Patients having diagnosed of COPD for at least 1 year, treated with inhalation devices and attained inhaler technique training were eligible for study. Demographic and clinical characteristics were obtained and inhaler techniques were assessed. The error was classified as critical or noncritical regarding medication reaching the lungs. Among 143 patients, 27 had history of exacerbation. The median inhaler devices per patients were 2 similarly in both groups. The proportion of patients performing at least 1 critical error was significantly lower in those having history of exacerbation and using pMDI without spacer ($p=0.020$) while the proportion of patients performing at least 1 error was significantly higher in those with history of exacerbation ($p=0.014$). History of exacerbation has no impact on inhaler technique except MDI without spacer. Continuing inhaler technique training and assessment are strongly recommended to sustain proper inhaler technique as well as increase quality of life and economic benefits.

INTRODUCTION

Chronic obstructive pulmonary diseases (COPD) is the major cause of chronic morbidity and will rank 7th of global burden of diseases in 2030 (Bousquet and Khaltaev, 2007). The estimated prevalence of COPD are 4-20% worldwide in adults over 40 years of age and 6.3% in Asian population (Bousquet and Khaltaev, 2007). Furthermore, it is the 4th most common causes of hospitalization and most economic burden among chronic diseases in elderly patients (Bousquet and Khaltaev, 2007). Exacerbation of COPD is “an acute event characterized by a worsening of the patient’s respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication” (Roisin and Vestbo, 2013). It accounts for two third

of the direct cost of COPD (Anzueto, 2010). Frequent exacerbations negatively impact on health aspects: lung function, exercise capacity, quality of life, morbidity and mortality (Anzueto, 2010) and socioeconomic aspects: inhaler and hospitalization cost (Capstick and Clifton, 2012). Therefore, the outcome of treatment is to minimize the impact of current exacerbation and to prevent the development of subsequent exacerbations (Roisin and Vestbo, 2013). Several treatment modalities are proposed to prevent exacerbation including the correct use of inhaler devices (Roisin and Vestbo, 2013).

However, inhaler handling error is common among COPD patients (Melani *et al.*, 2011) and the cooperation rate of inhaler therapy is much lower than other chronic diseases (Agh and Meszaros, 2012). There were 75% of COPD patients performed at least 1 critical error of inhaler handling leading to little or no medication reaching the lungs, (Pothirat *et al.*, 2015) and even higher to 90% in those with exacerbation (Ahmad *et al.*, 2013) but it could be reduced to 25% after training (Pothirat *et al.*, 2015).

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However, COPD patients experiencing this life threatening condition had a better response to education and management plan (Farkas *et al.*, 2011). Therefore, identification of poor inhaler technique becomes an essential part of the COPD management especially, re-assessment at the time of hospital discharge and 4 - 6 weeks later as recommended by Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2013 (Roisin and Vestbo, 2013). But sustaining correct inhaler technique after exacerbation is still controversy (Press *et al.*, 2012). This study aimed to determine the impact of exacerbation on the errors of inhaler techniques among COPD patients.

MATERIAL AND METHODS

This observational study was conducted in chest clinic at Central Chest Institute of Thailand. The study was approved by the Institute ethics committee. The previous study showed that 75% of COPD patients performed at least 1 error across 4 different types of inhaler devices (Pothirat *et al.*, 2015). In our study, at least 5 types of prescribed devices were expected then patients performed at least 1 error was estimated to be 90% with a 95% confidence interval and the precision to be within 5% of the true value. In order to compare inhaler techniques between patients with and without exacerbation, the estimated ratio of was based on 21 % hospitalization rate among COPD patients (Bollu *et al.*, 2013). Therefore, the sample size of at least 138 patients with the ratio of 1:4 for patients with and without exacerbation was required for this study.

Study participants

Patients having diagnosed as COPD for at least 1 year, treated with inhalation devices, attained inhaler technique training by pharmacists either at regular appointment or before hospital discharge were eligible for study. Exclusion criteria were having co-morbidity of cardiovascular diseases, asthma or lung cancer and unable to co-operate in assessment of inhaler devices. Study information was provided by verbal and participant information sheets to all patients before obtaining written informed consent.

Study Procedures

Face-to-face interview was conducted to obtain demographic characteristics while clinical characteristics were obtained from medical records. Patients were asked to demonstrate inhaler technique for each currently prescribed inhalers containing placebo and were assessed using inhaler technique checklists (Allen, 1997; Ho *et al.*, 2004; Batterink *et al.*, 2012).

Statistical Methods

Categorical variables were summarized as frequencies and percentages, and then analyzed using the chi square test or the Fisher's exact test. Continuous variables were summarized as mean and standard deviation or median and interquartile range (IQR) values and compared using t-test or the Mann-Whitney U-test where appropriate. The multiple logistic regression was

performed on the variables with significant differences between patients with and without exacerbation using overall errors as the dependence variable. All tests for significance were two-sided and $p < 0.05$ was considered statistical significance.

Definitions

GOLD classification (Roisin and Vestbo, 2013): the spirometric classification of airflow limitation: GOLD 1, mild; GOLD 2, moderate; GOLD 3, severe; and GOLD 4, very severe.

Critical error (Batterink *et al.*, 2012; Allen, 1997; Ho *et al.*, 2004): step of which incorrect performance would lead to little or no medication reaching the lungs.

Multiple devices: prescribed inhaler ≥ 2 devices for each patient.

RESULTS

Socio-demography

The totals of 143 patients were enrolled in the study. There were 27 patients (23.28%) with history of exacerbation. Of these, 10 patients had frequent exacerbations (2 exacerbations per year). Majority of patients were male similarly in both groups (92.6% vs 93.10%, $p=1.000$). They were elderly and those with history of exacerbation were slightly younger (median (IQR) = 69.00 years (62.00-76.00) vs 71.50 years (65.00-77.00), $p=0.295$). Most of them were married (85.20% vs 76.70%, $p=0.337$), having low education level (73.10% vs 71.40%, $p=0.869$) and low income (80.80% vs 70.30%, $p=0.292$) similarly in both groups. Disease severity was significantly different between both groups ($p=0.010$) and the proportion of patients with severe disease (GOLD 3 and 4) was significantly higher in exacerbation group (39.60% vs 70.30%, $p=0.004$) (table 1).

Inhaler devices

There were 5 different types of prescribed inhaler devices: pressurized metered dose inhaler (pMDI) with and without spacer, turbuhaler, accuhaler and handihaler. The median prescribed inhaler devices per patients (IQR) were 2 similarly in both groups (2 (2.00-2.00) vs 2 (2.00-2.50), $p=0.270$). Proportion of patients using multiple devices was significantly higher in patients with history of exacerbation (78.40% vs 100.00%, $p=0.004$). The pMDI without spacer and accuhaler were the most common devices prescribed in both groups. The latter had significantly higher proportion in patients with history of exacerbation (85.20% vs 64.70%, $p=0.039$) while turbuhaler was the less common similarly in both groups (3.70% vs 7.76%, $p=0.687$) (figure 1). Long acting B₂ agonists and inhaled corticosteroids were the most common prescribed inhalers with the significantly higher proportions in exacerbation group ($p=0.004$ and $p=0.014$) (figure 2).

Generally, proportion of patients performing at least 1 error was significantly higher in those with history of exacerbation (100% vs 81.90%, $p=0.014$) while proportion of patients performing at least 1 critical error was similar in both groups

(59.30% vs 53.40%, p=0.585). However, among those using pMDI without spacer, proportion of patients performing at least 1 critical error was significantly lower in exacerbation group (4.80% vs 29.20%, p=0.020). Patients using turbuhaler showed the highest error and critical error rates in both groups (table 2) and the step of

loading a dose was the most common mistake (table 3). After controlling for confounders, critical error of pMDI without spacer was 0.04 times lower (95%CI=0.003-0.60, p=0.020) and number of prescribed medications was 10.85 times higher in patients with history of exacerbation (95%CI=1.69-69.51, p=0.012).

Table 1: Demographics and clinical characteristics of COPD patients.

Variables	n	History of exacerbation				p value
		n	No n (%)	n	Yes n (%)	
Male	143	116	108 (93.10)	27	25 (92.6)	1.000
Age (year); median (IQR)	143	116	71.50 (65.00-77.00)	27	69.00 (62.00-76.00)	0.295
Married	143	116	89 (76.70)	27	23 (85.20)	0.337
Senior high school and lower; n (%)	117	91	65 (71.40)	26	19 (73.10)	0.869
Low income (<5000 bath)	117	91	64 (70.30)	26	21 (80.80)	0.292
Smokers	128	103		25		1.000
Current smokers			6 (5.80)		1 (4.00)	
Ex-smokers			97 (94.20)		24 (96.00)	
Duration of COPD (years) ; median (IQR)	143	116	4.00 (2.00-8.00)	27	4.00 (2.00-8.00)	0.874
Severity	143	116		27		0.010
GOLD 1			19 (16.40)		3 (11.10)	
GOLD 2			51 (44.00)		5 (18.50)	
GOLD 3			33 (28.40)		12 (44.40)	
GOLD 4			13 (11.20)		7 (25.90)	
Number of inhaler devices; median (IQR)	143	116	2 (2.00-2.00)	27	2 (2.00-2.50)	0.270

Table 2: Inhaler devices and at least 1 overall and critical error in COPD patients with and without history of exacerbation

Inhaler devices	n	Overall errors		p value	Critical errors		p value	
		no exacerbations	n exacerbations		n no exacerbations	n exacerbations		
pMDI (n=93)	72	53 (73.60)	21 17 (81.00)	0.493	72	21 (29.20)	21 1 (4.80)	0.020
pMDI with spacer (n=52)	43	22 (51.20)	9 3 (33.30)	0.469	43	20 (46.51)	9 6 (66.70)	0.465
Turbuhaler (n=10)	9	8 (88.90)	1 1(100.00)	1.000	9	5 (55.6)	1 1(100.00)	1.000
Accuhaler (n=98)	75	56 (74.40)	23 18 (78.30)	0.726	75	35 (46.70)	23 15 (65.20)	0.119
Handihaler (n=33)	23	13 (56.50)	10 9 (90.00)	0.109	23	2 (8.70)	10 1 (10.00)	1.000
All devices (n=143)	116	95 (81.90)	27 27 (100.00)	0.014	116	62 (53.40)	27 16 (59.30)	0.585

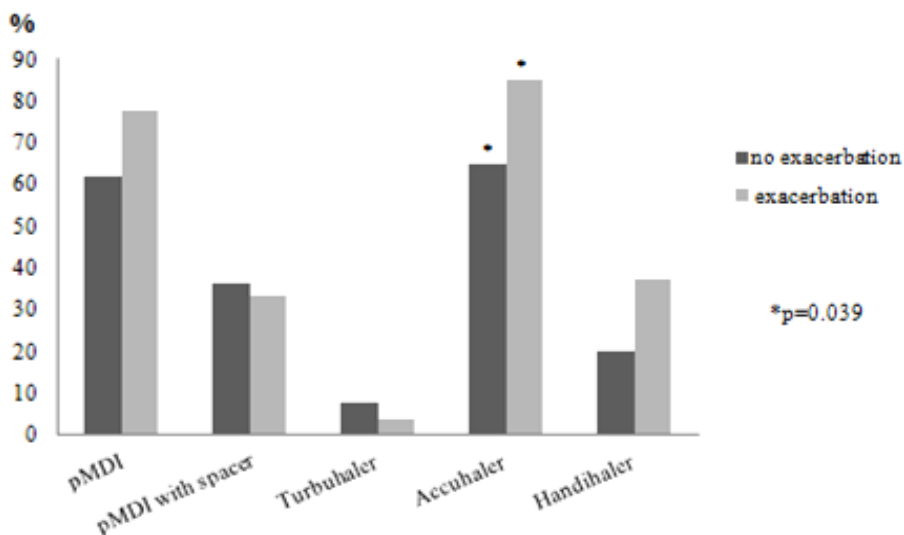


Fig. 1: Inhaler devices prescribed in COPD patients with and without history of exacerbation.

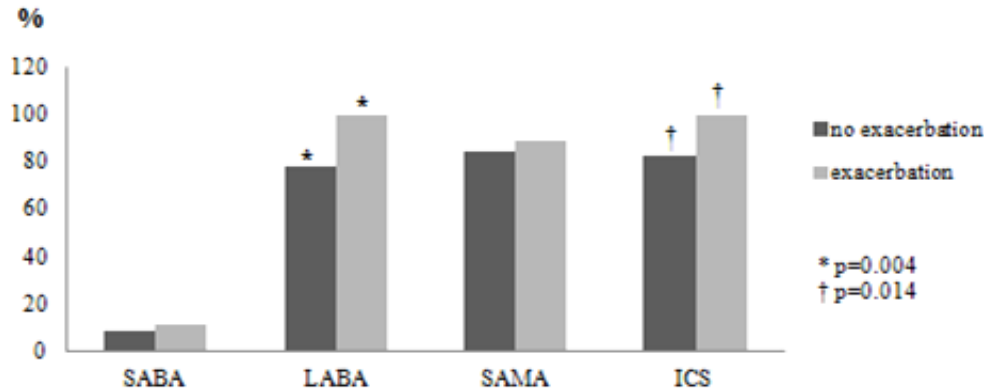


Fig. 2: Pharmacologic classifications of inhalers prescribed in COPD patients with and without history of exacerbation. (SABA: Short acting B₂ agonist, LABA: Long acting B₂ agonist, SAMA: Anticholinergic+B₂ agonist, ICS: inhaled corticosteroids)

Table 3: Incorrect steps of inhaler devices in COPD patients with and without history of exacerbation.

History of exacerbation	pMDI (n=72/21)		pMDI with spacer (n=42/9)		Turbuhaler (n= 9/1)		Accuhaler (n=75/23)		Handihaler (n=23/10)	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Shake thoroughly*	20 ^a (27.80)	1 ^a (4.80)	16 (38.10)	2 (22.20)	NA	NA	NA	NA	NA	NA
Remove capsule from blister and place in chamber*	NA	NA	NA	NA	NA	NA	NA	NA	1 (4.30)	0
Hold in upright position or horizontally (and press green piercing button in once and release) *	1 (1.40)	1 (4.80)	0	0	0	0	14 (18.70)	7 (30.40)	1 (4.30)	0
Insert inhaler into spacer*	NA	NA	1 (2.40)	0	NA	NA	NA	NA	NA	NA
Twisting grip to right and then back until click is heard*	NA	NA	NA	NA	1 (11.10)	1 (100.00)	NA	NA	NA	NA
Open using thumb grip and load dose by sliding lever until it clicks*	NA	NA	NA	NA	NA	NA	1 (1.30)	1 (4.30)	NA	NA
Breath out gently (away from mouthpiece) *	33 (45.80)	8 (38.10)	26 ^b (61.90)	1 ^b (11.10)	5 (55.60)	0	20 (26.70)	9 (39.10)	9 (39.10)	6 (60.00)
Close lips on mouthpiece or hold 3-4 cm. away from mouth	4 (5.60)	0	2 (4.80)	2 (22.20)	0	0	1 (1.30)	0	2 (8.70)	0
Press down firmly on canister once and/or breath in slowly and deeply*	2 (2.80)	0	1 (2.40)	1 (11.10)	NA	NA	1 (1.30)	0	0	1 (10.00)
Hold breath for at least 10 seconds*	16 (22.20)	2 (9.50)	0	0	2 (22.20)	0	0	0	7 (30.40)	2 (20.00)
Breath out gently (away from mouthpiece)	0	0	13 (31.00)	2 (22.20)	3 (33.30)	0	17 (22.70)	4 (17.40)	5 ^c (21.70)	7 ^c (70.00)
If an extra dose is needed, wait 1 minute and then repeat steps	36 (50.00)	13 (61.90)	0	0	8 (88.90)	0	48 (64.00)	15 (65.20)	11 (47.80)	8 (80.00)
Rinse your mouth with water after each use of the inhaled steroids*	0	2 (66.70)	0	0	3 (33.30)	0	9 (12.00)	1 (4.30)	0	0

^ap=0.035, ^bp=0.008, ^cp=0.016 *critical step, NA=not applicable.

DISCUSSION

Most of COPD patients in this study were elderly with low education level and income similar to global report (Bousquet and Khaltayev, 2007). Proportion of patients performing at least 1 error (85.31%) was higher than previous studies (74.80%) (Pothirat *et al.*, 2015) due to higher proportion of patients with multiple devices in this study (78.40% vs 69.90%) (Pothirat *et al.*, 2015). Proportion of patients performing at least 1 critical error and having history of exacerbation (59.3%) was not different to the hospitalized patients (59.0%) in previous study (Batterink *et al.*, 2012). Patients performing at least 1 critical error possess the high risk of re-exacerbation since at least 1 critical error was

associated with 50% increment of hospitalization or emergency department visit (Price, 2014).

The highest proportion of patients with at least 1 error and critical error were found in those using turbuhaler similar to previous study (Sriram and Percival, 2015). The pMDI without spacer was the most common device prescribed in this study supported previous studies (Batterink *et al.*, 2012; Pothirat *et al.*, 2015). It was associated with the utmost error among hospitalized patients (Batterink *et al.*, 2012) while spacer enhanced its correct technique in patients with exacerbation (Pothirat *et al.*, 2015). This study showed that history of exacerbation significantly reduced critical errors of pMDI without spacer though it is quite difficult to use, requires good hand-breath coordination and hand or finger

muscle strength (Yawn *et al.*, 2012). Short acting bronchodilator, one of the recommended management and prevention of severe exacerbation (Criner, 2015) is commercially available in pMDI then it is the crucial target for technique trainings and evaluation.

The intensive and repeated training during hospitalization can promote the correct technique. Moreover, exacerbation significantly increased adherence to the devices especially, the one relieving breathlessness (Wisniewski *et al.*, 2014). On the other hand, the errors of other devices could not decrease since many risk factors of technique errors: old age with poor recognition, low education, multiple medications and devices (Bonini and Usmani, 2015, Micalef, 2015) were common in our patients. Furthermore, insufficient knowledge of inhaler techniques (Baverstock, Woodhall, and Maarman, 2010) and lack of attention in teaching and checking inhaler techniques (Anonyms, 2012) among health care professionals in the real clinical practice may involve these errors.

Several methods are strongly recommended for improving inhaler technique. Firstly, individualizing inhaler choice regarding patient's physical ability was shown to enhance good inhaler techniques (Chorao *et al.*, 2014). Secondly, demonstration was proved to be better than verbal and written instructions (Yawn *et al.*, 2012, Capstick and Clifton, 2012). The "teach back method" or patients' showing their inhaler techniques was strongly recommended (Dantic, 2013). Inhaler training aids should be used to assist training and assess techniques to ensure significant lung deposition (Capstick and Clifton, 2012). Thirdly, inhaler technique training is the continuous process. It is not time consuming since it can be as short as a few minutes with regular training (Capstick and Clifton, 2012). Lastly, the transitional care either different locations or different levels of care in the same location must be well established.

COPD patients with acute exacerbation showed no improvement in quality of life in the first 10 days after treatment and at 6 month after acute exacerbation, half of them even rated their health status as fair to poor and required carers for daily activities (Anzueto, 2010). Moreover, quality of life decreased significantly (Agrawal *et al.*, 2015; Prakash *et al.*, 2014) while risk of exacerbation increased significantly in severe and very severe COPD (Roisin and Vestbo, 2013). In this study, the mean time after acute exacerbation was 5.3 months and 70.30% of patients in exacerbation group were classified as severe and very severe COPD. Therefore, these patients were most likely to have poor quality of life and high risk of re-exacerbation. In addition, proportion of patients using multiple devices as well as costly inhaled therapy such as long acting B₂ agonists and corticosteroids was significantly higher in exacerbation group. Thus these patients were strongly associated with high socioeconomic burden supported previous studies (Anzueto, 2010). Correct inhaler technique can ameliorate those problems. However, this study has some limitations. The errors of inhaler technique may be underestimated since some steps were difficult to evaluate through observation.

CONCLUSION

History of exacerbation has no impact on inhaler technique except for MDI without spacer. Inhaler technique training and assessment are strongly recommended to continue throughout the period of inhalation therapy. Improving inhaler technique can further decrease exacerbation rate as well as increase patients' quality of life and economic benefits.

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