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Is Inhaler Technique Associated with Quality of Life in Patients with Chronic Obstructive Pulmonary Disease?

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ABSTRACT

Background: Inhalers are the mainstay of treatment for patients suffering from chronic obstructive pulmonary disease. However, incorrect inhaler technique is a considerable challenge.

Objective: We aimed to evaluate inhaler technique and its association with quality of life in a sample of patients with chronic obstructive pulmonary disease.

Methods: This cross-sectional study included patients with confirmed chronic obstructive pulmonary disease who were prescribed at least 1 inhaler medication on a regular basis. Patients were recruited from the outpatient pulmonary clinic of a hospital in Tehran. Inhaler technique was assessed according to a validated checklist. Patients' quality of life was evaluated using Chronic Obstructive Pulmonary Disease Assessment Test.

Results: One hundred seventy-five patients with mean (SD) age of 59.0 (10.1) years were included. Patients' devices were 192 (62.3%) pressurized metered-dose inhalers (including pressurized metered-dose inhalers plus spacer) and 116 (37.7%) dry powder inhalers. Unfortunately, only 2.86% of patients used their inhalers completely correct. The highest rate of errors was committed by patients who used metered-dose inhalers plus spacer. Patients with a higher educational degree had significantly lower rate of errors on average ($P=0.001$). The most frequent errors made by patients using pressurized metered-dose inhalers or Turbuhaler was priming the inhaler before the first administration in 90.6% and 78.3% of patients, respectively. Chronic Obstructive Pulmonary Disease Assessment Test scores in patients using different inhaler devices were not significantly different. However, in patients with lower quality of life, significantly more patients had poor inhaler technique ($P=0.0001$).

Conclusions: There is still considerable need for interventions to optimize inhaler technique. We also noted that appropriate inhaler technique is associated with better quality of life. (*Curr Ther Res Clin Exp.* 2020; 81:XXX-XXX)

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Introduction

Chronic obstructive pulmonary disease (COPD) is a condition that is mainly associated with airflow limitation and respiratory

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symptoms.¹ It is estimated that COPD will be the fourth leading cause of death in 2030 worldwide, a 1-step move up in the rank order compared with 2002.² The prevalence of the disease was reported to be 4.9% in Iran³ and 9.2% in Tehran.⁴ It was also demonstrated that patients with COPD have 50% lower long-term survival compared with their healthy counterparts.⁵ Additionally, COPD costs considerably for both patients and health care systems. Medication and non-medication costs of COPD management increase as the disease progress. The annual expenses of disease

management for a patient with lower-stage disease is about \$1700 and in higher stages, this could reach to around \$11,000.⁶ Although a higher portion of the expenses are spent for hospital care,^{5,6} outpatient care and medications can also cost an average of \$900 and \$2000 annually, respectively.⁵

Medications delivered through airways are among the modalities for controlling symptoms in COPD. This way of drug delivery has several advantages over the systemic route, such as providing higher medication concentrations in lungs, faster response rate, and lower possibility of systemic adverse effects.⁷ Several inhaler devices are now available in the Iranian drug market. Generally, pressurized metered-dose inhalers (pMDIs) are the most frequently used devices worldwide due to their acceptable cost, effectiveness, and simple technique.⁸ Although inhaled medications are considered the optimal route and gold standard for the treatment of COPD, their delivery to the site of action can be challenging. In fact, most patients are not able to use the devices correctly without training and some cannot use them properly despite education.^{7,8} It has been proposed that patients' technique of using devices can lead to a significant difference in clinical response even between pMDIs and dry powder inhalers (DPIs) despite their similar efficacy in correct use.⁹ In a systematic review of the studies published between 1975 and 2014, a high prevalence of inappropriate device use among patients with pulmonary disorders was noted.¹⁰ Additionally, in patients who use spacers, despite advantages regarding inhalation method and better drug delivery,^{11,12} the new incorrect technical errors as well as the increased cost are drawbacks.¹¹ Moreover, if patients use their pMDI properly, the spacers do not provide additional benefit in bronchodilation.¹² However, more disappointing findings indicate that health care professionals themselves have poor/suboptimal knowledge regarding inhaler technique, which can consequently influence patients' device use technique.^{13,14} In a study of patients with COPD, only 22% reported complete confidence regarding proper use of their inhaled medications. Higher confidence was associated with higher adherence and lower COPD Assessment Test (CAT) scores, showing better health status.¹⁵ The importance of the inhaler technique is more elucidated considering the fact that the outcome of inhaler therapy is reliant on the accurate administration technique not the device selected.¹⁶ Unfortunately, studies that focus on the evaluation of the inhalation technique are scarce in Iran and most of them did not include patients with COPD.^{17–19}

CAT score was developed to provide a short, valid, reliable, and simple tool for the assessment of health status as well as monitoring and follow-up of patients with COPD. It evaluates 8 items, including cough, phlegm, chest tightness, breathlessness going up hills/stairs, activity limitation at home, confidence leaving home, sleep, and energy, which constitute main problems in various disease stages.²⁰ This self-completed questionnaire has been translated and validated in a Persian previously.²¹ A systematic review on the psychometric properties of the CAT concluded that the test is valid, reliable, and can be used in trials.²² CAT score is correlated with St George's Respiratory Questionnaire, a tool to evaluate health-related quality of life,²³ as well as the forced expiratory volume for 1 second expressed as a percentage of the forced vital capacity predicted values.^{24,25} Additionally, it was demonstrated that with effective management of COPD with inhaled medications, decrease in CAT score can be anticipated depending on baseline score.²³ However, studies on the association between inhaler technique and CAT score are scarce.²⁶ Pothirat et al²⁷ noted a significant role for CAT score ≥ 10 with incorrect technique in univariate regression analysis. Considering the importance of correct and proper inhaler technique, and high rates of errors committed by patients in this context, the current study was designed to evaluate the inhaler technique and its correlation with patients' quality of life measured by CAT score.

Materials and Methods

This study was a part of a research project in COPD patients in which the medication use of these patients and outcomes were evaluated.

Patients and study setting

This cross-sectional study was conducted from January to November 2015 in outpatient pulmonary clinic of in the Imam Khomeini Hospital Complex affiliated with Tehran University of Medical Sciences. The study was approved by the ethics committee of the university.

Patients with confirmed diagnosis of COPD who received at least 1 inhaled medication on a scheduled basis and willing to enter the study were included. Patients with acute exacerbation of COPD as well as those diagnosed with other respiratory pathologies or receiving supplemental oxygen therapy were excluded.

Data collection

Demographic data and a complete medication history were documented for each patient. Stage of the disease was classified into 4 stage categories based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD).

Assessment of quality of life

Patients' quality of life was evaluated using CAT.²⁰ This tool has been translated and validated in nearly 100 times worldwide.²⁸ It was previously translated and validated in Persian.²⁹

Assessment of inhaler technique

We used a separate checklist for each inhaler, in which a step-by-step proper use of the device was listed in separate items. To develop the checklists, we used different resources such as drug leaflets, previous articles,^{30,31} patient education materials provided by pharmaceutical companies, and online UpToDate (www.uptodate.com) for all of the available inhaler devices in the Iranian drug market. The checklists were then translated to Persian by a pharmacist and was revised by a clinical pharmacist. To validate these checklists, we presented them to a group of experts. The checklists were presented in 2 separate packages with a cover letter in which the aim of the study, as well as the requested evaluations were pointed. If the experts were willing to assess the second part, then it was handed to them. We aimed to ensure the correctness of items, the proper order of the items and necessity of separate assessment of each item (instead of merging some items together) through the experts' comments. In total, 6 clinical pharmacists and 2 pulmonologists assessed the checklists. Then, the experts' comments were evaluated and implemented in the checklists by 2 clinical pharmacists. Following this step, a pilot study on limited number of patients was conducted to test the checklists in practice. The checklists are presented in Supplemental Appendix 1. The sample devices were provided for patients based on their routine inhaler use. Patients were asked to use the inhalers as if it was a new device obtained from the pharmacy. The steps performed by patients were observed by the researcher and evaluated according to the checklist. In cases that a caregiver was administering or helping the patient in using the devices, the usual way of medication administration by the patient and caregiver were observed. After the assessments, in cases of observing errors, patients were educated regarding the proper use of the inhalers. In the assessment of patients using pMDIs, based on the need for repeating the dose, the number of items varied accordingly.

Table 1
Distribution of disease status and treatment-related factors among patients using different devices.

Characteristic	Inhaler				Total	
	pMDI	DPI	pMDI + spacer	pMDI + DPI		
Inhaler users [†]	57 (32.6)	38 (21.7)	19 (10.9)	61 (34.8)	175 (100)	
Age [‡] (y)	59.4 (9.9)	59.2 (8.6)	62.4 (9.3)	59.6 (11.3)	59.8 (10.1)	
Age range (y)	43-85	42-75	45-84	42-85	42-85	
Male sex [†]	35 (61.4)	21 (55.3)	7 (36.8)	38 (62.3)	101 (57.7)	
Education [†]	Illiterate	26 (45.6)	14 (36.8)	23 (37.7)	76 (43.4)	
	Under diploma	26 (45.6)	15 (39.5)	5 (26.3)	71 (40.6)	
	Diploma	3 (5.3)	7 (18.4)	0	11 (18.0)	21 (12)
	Academic	2 (3.5)	2 (5.3)	1 (5.3)	2 (3.3)	7 (4)
GOLD stage [†]	1	28 (49.1)	21 (55.3)	5 (26.2)	17 (27.9)	71 (40.6)
	2	19 (33.3)	11 (28.9)	9 (47.4)	32 (52.4)	71 (40.6)
	3	7 (12.3)	5 (13.2)	4 (21.1)	9 (14.8)	25 (14.3)
	4	3 (5.3)	1 (2.6)	1 (5.3)	3 (4.9)	8 (4.5)
CAT score [‡]	10.2 (7.0)	8.3 (7.8)	13.8 (9.4)	9.6 (7.9)	10.0 (7.9)	
CAT score reange [‡]	0-10 [†]	33 (57.9)	26 (68.4)	9 (47.4)	37 (60.7)	105 (60)
	11-20 [†]	16 (28.1)	8 (21.1)	5 (26.3)	19 (31.1)	48 (27.4)
	21-30 [†]	8 (14.0)	3 (7.9)	4 (21.0)	4 (6.6)	19 (10.8)
	31-40 [†]	0	1 (2.6)	1 (5.3)	1 (1.6)	3 (1.7)
	No. of inhalers [†]	1	8 (14.0)	9 (23.7)	1 (5.2)	0
Duration of inhaler use [†]	2	33 (57.9)	26 (68.4)	9 (47.4)	42 (68.9)	110 (62.9)
	3	15 (26.3)	3 (7.9)	9 (47.4)	18 (29.5)	45 (25.7)
	≤1 mo	1 (1.8)	0	0	4 (6.6)	5 (2.9)
	1-6 mo	23 (40.4)	18 (47.4)	7 (36.8)	24 (39.3)	72 (41.1)
	6-12 mo	16 (28.1)	9 (23.6)	3 (15.8)	21 (34.4)	49 (28)
1-3 y	7 (12.3)	7 (18.4)	7 (36.8)	8 (13.1)	29 (16.6)	
	3-5 y	5 (8.7)	2 (5.3)	0	0	7 (4)
	>5 y	5 (8.7)	2 (5.3)	2 (10.6)	4 (6.6)	13 (7.4)

CAT=Chronic Obstructive Pulmonary Disease Assessment Test; DPI=dry powder inhaler, GOLD=Global Initiative for Chronic Obstructive Lung Disease; pMDI=pressurized metered-dose inhaler.

[†] Values are presented as n (%).

[‡] Values are presented as mean (SD).

To calculate the incorrect rate for patients who used more than one inhaler devices, we divided the number of wrong items by the sum of the items of the checklists of all of the inhalers. Because the optimal drug delivery depends on the correct performance of each step, we weighted all of the steps as similarly important.³² We report the inhaler technique in 2 ways. First, perfect technique versus presence of at least 1 error. Second, we categorized patients to those with >30% and <30% incorrect rate in using inhalers.

Statistical analysis

Descriptive statistics were reported using frequency and percentage for qualitative variables and mean (SD) for quantitative ones. Comparing continuous variables between groups were performed using Kruskal-Wallis or Mann-Whitney tests. The χ^2 test was used to evaluate relation between 2 categorical variables. All analysis was performed using SPSS version 21.0 (IBM-SPSS Inc, Armonk, NY). *P* value < 0.05 was considered significant.

Results

Patients

In total, 175 patients with mean (SD) age of 59.0 (10.1) years were included in the study. Among the patients 101 (57.7%) were men. Most of patients were illiterate (n=76 [43.4%]) had earned less than a college degree (n=71 [40.6%]). Details of patients' characteristics and disease status are presented in Table 1.

Inhaler devices

Patients were using 308 devices (1.76 device per patient on average). Most of the patients (89.71%) used more than 1 device. These devices included 192 (62.3%) pMDIs (including pMDI plus

spacer) and 116 (37.7%) DPI devices. The most frequently used DPI devices were Revolizer (n=55 [17.9%]) followed by Turbuhaler (n=45 [14.6%]), Handihaler (n=6 [1.9%]), Aerolizer (n=5 [1.6%]) and Diskus (n=5 [1.6%]) (Table 1). Most of the patients (n=147 [84%]) were able to use their inhaler device without any help. Seventy-two percent of patients started using inhalers from <1 year ago. Duration of inhaler use was not significantly different between patients using different devices (*P*=0.15).

Quality of life

Mean (SD) of CAT score was 10.0 (7.9) and scores ranged from 0 to 39. In most of the patients (n=105 [60.0%]), the score was between 0 and 10. Similar findings regarding CAT scores was noted for patients using different inhalers (Table 1). Results of the Kruskal-Wallis test showed that there was no significant difference between CAT scores in patients using different inhaler devices (pMDI, MDI+ spacer, DPI, and pMDI + DPI).

Relation between CAT scores and other variables are summarized in Table 2. As expected, patients with higher stages of COPD also had significantly higher CAT scores (*P*=0.002). Slightly increased CAT score was found in patients with higher number of daily medications (including inhalers and noninhalers) (Spearman *r*, 0.16; *P*=0.03). Other variables were not significantly correlated with CAT score (Table 2).

Inhaler technique

Only 5 patients (2.86%) (3 men and 2 women) used their inhalers completely correct. The frequency of errors in using different devices is summarized in Table 3. Comparison of incorrect rate between different devices showed that the highest rate of errors was committed by patients who used a pMDI plus spacer (mean, 42.3%) followed by those who used only pMDI (mean,

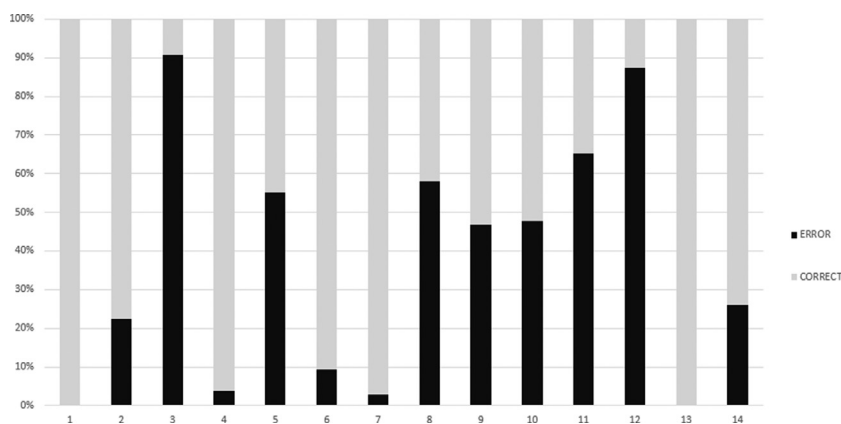


Figure 1. Frequency of errors made by patients in each step of the pressurized metered-dose inhaler (pMDI) checklist.

Table 2
Evaluation of association between different variables and Chronic Obstructive Pulmonary Disease Assessment Test (CAT) score.

Variable	No. of patients	CAT score*	P value
Sex			
Male	10	9.8 (7.5)	0.88
Female	74	10.1 (8.3)	
GOLD stage			0.002
1	71	8.0 (6.9)	
2	71	10.4 (7.9)	
3	25	11.1 (7.2)	
4	8	20 (9.4)	
Education			0.39
Illiterate	76	10.8 (8.4)	
Under diploma	71	9.6 (7.6)	
Diploma	21	7.5 (5.5)	
Academic	7	12.9 (9.3)	
Duration of inhaler use			0.40
≤1 mo	5	12.2 (10.4)	
1–6 mo	72	8.8 (7.0)	
6–12 mo	49	10.2 (7.9)	
1–3 y	29	10.3 (9.5)	
3–5 y	7	12.1 (8.8)	
>5 y	13	12.8 (6.4)	
Smoking			0.85
Current smoker	82	9.8 (7.9)	
Exsmoker	62	10.3 (7.9)	
Nonsmoker	31	9.9 (7.8)	

GOLD = Global Initiative for Chronic Obstructive Lung Disease.

* Values are presented as mean (SD).

38.9%) (Kruskal-Wallis test $P=0.001$). Details of inhaler technique is presented in Figures 1 through 4 and Supplemental Appendix 2.

Table 3
Characteristics of patients with at least 1 error and those with >30% incorrect rate in inhaler technique.

Characteristic	% of error (Mean [SD])	At least 1 error		>30% error rate	
		n (%)	P value	n (%)	P value
Sex					
Male (n = 101)	28.3 (17.8)	98 (97.0)	0.91	40 (40)	0.51
Female (n = 74)	27.6 (15.3)	72 (97.3)		26 (35.1)	
Education			0.24		0.024
Illiterate (n = 76)	32.0 (16.7)	75 (98.7)		38 (50)	
Under diploma (n = 71)	27.1 (16.3)	69 (97.2)		22 (31.4)	
Diploma (n = 21)	20.6 (15.6)	19 (90.5)		5 (23.8)	
Academic (n = 7)	16.5 (13.8)	7 (100)		1 (14.3)	
Duration of inhaler use			0.90		0.37
≤1 mo (n = 5)	17.9 (11.3)	5 (100)		0	
1–6 mo (n = 72)	26.6 (16.3)	70 (97.2)		25 (35.2)	
6–12 mo (n = 49)	27.2 (15.8)	48 (98.0)		18 (36.7)	
1–3 y (n = 29)	29.6 (18.8)	28 (96.6)		13 (44.8)	
3–5 y (n = 7)	40.7 (12.7)	7 (100)		4 (57.1)	
>5 y (n = 13)	32.2 (19.4)	12 (92.3)		6 (46.2)	
GOLD stage			0.69		0.47
1 (n = 71)	26.2 (17.9)	68 (95.8)		23 (32.4)	
2 (n = 71)	28.2 (16.3)	69 (97.2)		27 (38.6)	
3 (n = 25)	31.5 (15.2)	25 (100)		12 (48)	
4 (n = 8)	31.7 (14.3)	8 (100)		4 (50)	
CAT			0.33		<
0–10 (n = 105)	26.2 (16.5)	100 (95.2)		10 (9.5)	
11–20 (n = 48)	27.9 (15.9)	48 (100)		5 (10.4)	0.001
21–30 (n = 19)	37.9 (18.7)	19 (100)		9 (47.4)	
31–40 (n = 3)	29.6 (11.8)	3 (100)		0	

CAT = Chronic Obstructive Pulmonary Disease Assessment Test; GOLD = Global Initiative for Chronic Obstructive Lung Disease.

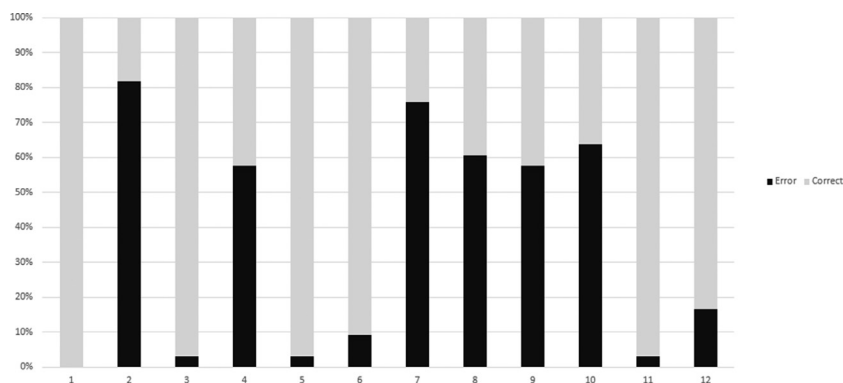


Figure 2. Frequency of error made by patients in each step of the pressurized metered-dose inhaler (pMDI) plus spacer checklist.

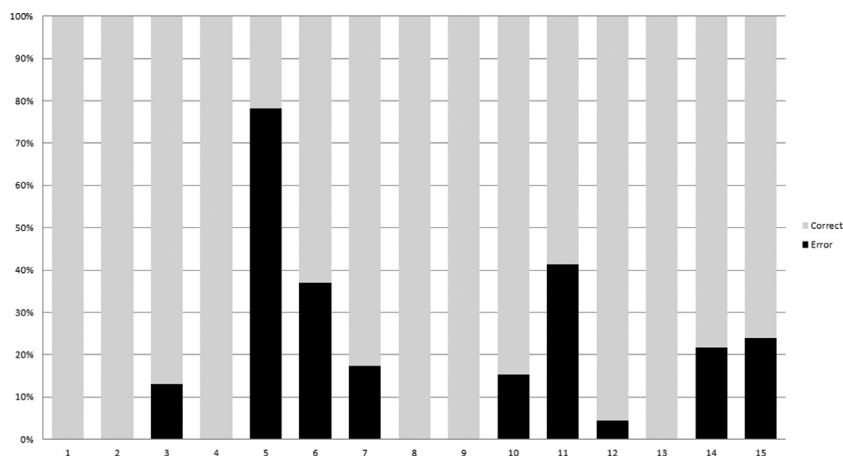


Figure 3. Frequency of error made by patients in each step of the Turbuhaler checklist.

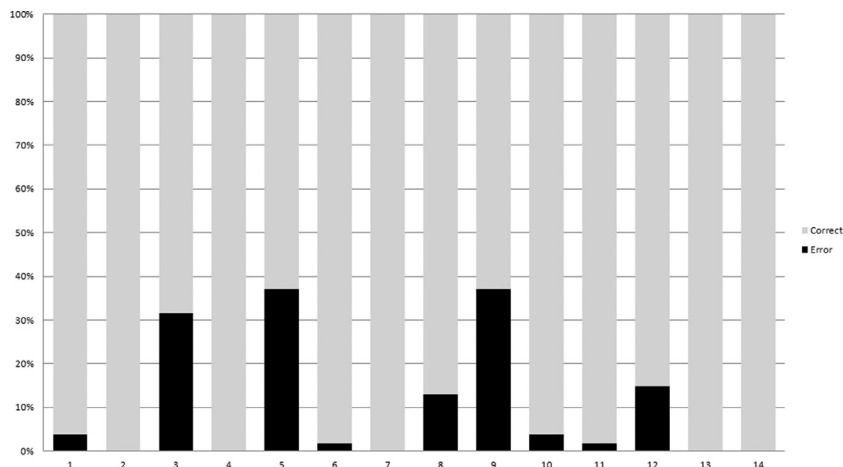


Figure 4. Frequency of error made by patients in each step of the Revolizer checklist.

errors made by patients in using their pMDI devices were regarding priming the inhaler before the first administration (90.6%), shaking the device before the second puff (87.4%), separating inhalation of each dose by 15 to 30 seconds (65.3%), and pressing the canister correctly to release the medication (57.9%). In another study in patients with COPD, it was demonstrated that shaking the inhaler was the second most frequent error in using pMDIs (52.3%), preceding breathing out gently to residual volume.²⁷ However, the last mentioned error was the fifth frequent step based on our results and shaking the pMDI was only 22% prevalent.

Table 4

Average errors in patients using different inhalers.

Inhaler device	No. of patients	Mean % of errors (SD)	Without error
pMDI	57	38.9 (15.8)	0 (0)
pMDI + spacer	19	42.3 (13.9)	0 (0)
DPI	38	15.4 (10.5)	2 (5.3)
pMDI + DPI	61	21.3 (11.6)	3 (4.9)

DPI = dry powder inhaler; pMDI = pressurized metered-dose inhaler.

The high frequency of priming error (spraying 1–4 puffs out) found in the current study, might be attributed to the inclusion of this item in the checklist in contrast with several other investigations.^{27,30,31,33} Despite the emphasis on this point in educational materials,³⁴ it seems that this item is neglected in the studies that assess the inhaler technique. Moreover, we evaluated patients' performance of the steps needed for optimal use of the second puff of pMDI, if they were ordered to do so by a physician. In fact, we included these steps in our assessment. At the end of the corticosteroid inhaler use, we noted that only 26% of patients rinse their mouth.

Our investigation showed that the mean percentage of errors was higher in patients using pMDI plus a spacer device compared with patients using pMDI devices alone. The most prevalent errors detected in these patients included priming the pMDI device (88.8%), actuating the device and breathing (75.8%), repeating the steps for the second puff inhalation (63.6%), and holding breath and exhaling normally (60.6%). In another study, Gregoriano et al³³ reported that among patients using pMDI with or without a spacer, 37% committed errors in shaking the inhaler before actuation as the most prevalent error.

In contrast to our findings, there are previous studies showing that using pMDI with a spacer is associated with lower rates of errors in inhalation technique.^{27,33} Additionally, in a study on patients diagnosed with COPD or asthma, patients made more mistakes using pMDIs compared with other types of inhaler devices such as DPIs.¹² A systematic review on errors in inhaler use also reported that pMDI users made significantly more mistakes compared with patients using other types of devices. However, despite evaluating different types of inhaler chambers they could not show that the addition of holding chambers to the pMDIs can decrease the errors substantially.¹⁰ Moreover, it was previously demonstrated that unless a patient rinses his or her mouth following the inhalation, the spacer may not add benefits to the use of pMDIs because medication deposition from mouth mucosa can be absorbed systemically.³⁵ The findings of the current study can be interpreted as an evidence that addition of the spacer to the pMDI may result in more mistakes and make the disease control more difficult in some patients. This is in contrast with the main aim of using the spacers and the comments suggesting their use by elderly patients.³⁶

The importance of correct inhaler technique is more pronounced considering the fact that among elderly patients with COPD, a substantial percentage cannot achieve the peak inspiratory flow with DPIs.³⁷ In patients using Turbuhaler, the most frequent error was omitting the priming of the inhaler by 78.3% of patients. This results in dose loading error and was the most frequent error found in another study.³⁸ However, this step was not included among the assessment checklists of several studies.^{30,31,33,39}

We found that the percentage of patients with incorrect technique in our study (>97%), was considerably higher compared with the previous reports. For example, Pothirat et al²⁷ noted that almost 75% of patients made at least 1 error. In another study, Arora et al¹² in India found that 82.3% of patients with asthma and COPD made at least 1 error. The high prevalence of inhaler technique error found in our study can be attributed mainly to the more detailed checklists used for evaluation. We aimed to have a comprehensive view of the inhaler use, including the second puff use, mouth rinse following inhaled corticosteroids, and patients' understanding of when to start a new Turbuhaler. In fact, among the advantages of the currently used checklists was the structured process of obtaining expert opinion regarding the items. Due to the variation in the assessment checklists of different studies, it seems that there is a need for a common validated assessment technique checklist to help better comparison of different patient populations.

When we investigated the role of literacy, we found that patients with more education had significantly lower rate of errors on average. Most patients evaluated in the current study were illiterate or were not highly educated. This could make it difficult for them to follow written instructions and could play a role in increasing the rates of errors. This finding is similar to previous studies.²⁷

We did not find a significant difference between the duration of using inhalers with inhaler errors. This finding could be interpreted as the need for continuous educations for patients.⁸

As expected, we found that mean CAT score in patients with different GOLD stages differed significantly. We noted that the error rate of >30% significantly differed among patients with different CAT score categories, but not GOLD stage. This finding is in keeping with a previous study that reported a significant association between CAT score and incorrect inhaler technique in patients with COPD.³³ We found that the difference between CAT scores of patients using different kinds of devices was not significant. This could magnify the effect of inhaler technique errors on disease control and indicates that the proper use of a device might be of greater importance than the type of device.

It was demonstrated that with an increase in the number of inhalers, error rate increases moderately. The increased variety of the devices or their numbers could confuse patients or affect on their compliance and increase the frequency of mistakes.

Limitations

This study has several limitations. First of all, we did not document the hearing or vision problems of patients that might have a considerable influence on patients' ability to follow verbal or written instructions. Additionally, we could not clearly document the source of patient education for their inhaler use. Despite a question in this regard, our patients were not able to distinguish different health care professionals such as physicians, nurses, or pharmacists from each other and we could not analyze the data. Moreover, data regarding the exacerbation history of patients that could help us to find its association with CAT score or inhaler technique was not available.

Conclusions

This study showed that there is still a long way to go to have standard inhaler technique. Priming of the inhalers is part of the correct technique that needs to be addressed in patient educational materials and assessments. We noted that performing >30% error in using an inhaler is higher among patients with higher CAT category.

Declaration of Competing Interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.curtheres.2020.100608.

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