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The effect of cognitive functions on the ability to learn how to use a Diskus device in patients with chronic obstructive pulmonary disease

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Abstract:

OBJECTIVE: Dry powder inhalers are a group of inhaled medications commonly used for the treatment of chronic obstructive pulmonary disease (COPD). Although they can be more easily administered than metered dose inhalers, there is a high rate of errors in device use. The present study aims to evaluate the relationship between the ability to learn how to use a Diskus device and cognitive functions in patients with COPD.

MATERIALS AND METHODS: The study included 30 inhaler-näive patients who were newly diagnosed with COPD. During their first visit, patients were administered a broad array of standardized neuropsychological tests and given a training on inhaler use. During the second visit, patients were divided into two groups according to their performance in the use of Diskus device: effective and ineffective.

RESULTS: Twenty-nine patients who completed the study showed a negative correlation between the cognitive test scores and Diskus training parameters. The number of errors and duration of training increased as the cognitive scores decreased. In Visit 2, a comparison between patients with ineffective and effective use of the Diskus device showed that cognitive function scores were higher in those with effective use.

CONCLUSIONS: Evaluation of cognitive functions in COPD patients is important in establishing an effective inhalation treatment.

Keywords:

Chronic obstructive pulmonary disease, cognitive function, dry powder inhalers

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Introduction

The therapeutic effect of inhaled medications is directly associated with delivery of the medication into middle and small airways. Regardless of their design, these medications should be administered using an appropriate technique. Even an optimal inhaler technique enables only 15%–30% of inhaled drugs reach target airways while it can be reduced to subtherapeutic levels with an inappropriate technique.[1-3] Patients find breath-actuated dry powder inhalers (DPIs) easier to use than pressurized metered-dose inhalers (MDIs). The Diskus device is one of the common DPIs used by chronic obstructive pulmonary disease (COPD) patients for topical administration of both inhaler bronchodilators and corticosteroids in the lower respiratory tract. However, rate of ineffective inhalation was high particularly in older patients despite training on inhalation technique with this group of agents.[4]

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Cognitive impairment is an important but often overlooked comorbidity in COPD. Cognitive impairment was shown both in hypoxemic and nonhypoxemic COPD patients, and magnetic resonance imaging studies showed cerebral hypoperfusion associated with cognitive dysfunction in this patient group.[5,6] Competent use of inhaled medication requires multistage motor tasks; and thus, cognitive dysfunction may lead to inefficiency in respiratory therapy, which is very important for COPD patients. Several studies have previously shown an association between the inhaler administration technique and cognitive functions, particularly in the elderly population and mainly in the MDI group.[7-9]

The objective of the present study was to evaluate the relation between the ability to learn and use a Diskus device and cognitive functions in COPD patients who were recently diagnosed and inhaler-näive. In addition to previous studies, we used more cognitive tests due to relation with frontal functions, assessed learning of patients with respect to both specific and motor learning processes, and also evaluated patients' performance in device use in the long-term.

Materials and Methods

Participants

The study included 30 consecutive newly diagnosed and inhaler-näive COPD patients. The study was approved by the Institutional Ethics Committee, and all patients signed informed consent documents. The diagnosis of COPD was based on clinical history, symptoms, and a postbronchodilator ratio of the forced expiratory volume in 1 s (FEV_1) to the forced vital capacity of <0.70 as recommended by international guidelines.[10]

Any patients with COPD exacerbations, low literacy skills, visual or auditory problems, focal neurological loss, and manual dexterity problems were excluded from the study.

Neuropsychological tests

We used a broad array of standardized neuropsychological tests including Mini-Mental State Examination (MMSE)[11,12] trail making Test A and B,[13] clock drawing,[14] forward and backward digit span tests, Brown–Peterson test,[15] verbal fluency test,[16] and geriatric depression scale.[17] All of these tests have been already adapted to the Turkish language with a high psychometric validity and reliability.

Mini mental state examination

This questionnaire measures general cognitive impairment and it is extensively used in clinical research.[11,12]

Trail making Test A and B

Trail making test measures impairment in executive cognitive functions, specifically disruption in attention and working memory. There are two parts in this test. In both of the tests, letters and numbers are located randomly on a piece of paper. In Part A, participants connect numbers in ascending order (1, 2, 3…). In Part B, participants alternately connect numbers and letters in ascending order (1, A, 2, B…). Time to complete Part A and Part B (recorded separately) is used as a score.[13]

Clock drawing

This test is commonly used to assess disruption in concentration and motor planning. Participants are asked to draw an analog clock. The analog clock must show ten past eleven. They are scored with completeness and correctness of drawing. The total score is 4 pts. They get a point for a circle (1 pt.), if all numbers are included (1 pt.), if they placed the numbers in the correct position (1 pt.), and place the hands correctly (1 pt.).[14]

Forward and backward digit span tests

These tests measure short-term and working memory capacity. In the forward span task, participants are asked to repeat a sequence of digits in the correct order. In the backward span task, they are asked to repeat the sequence in the reverse order. The number of trials remembered correctly used as the score of the test. Maximum score is 16 and 14 in the forward and backward digit span tests, respectively.

Brown–Peterson test

This test is designed to measure working memory capacity. Working memory capacity is related with our ability to hold information in the face of distractors. A consonant trigram and a three-digit number are given to participants. Participants count backward from the number aloud for 0, 9, 18, or 36 s. Then, they must recall the trigram.[15]

Verbal fluency test

This test measures the disruption in language functions. Participants are asked to generate as many words as possible. In the 1st three sessions, the words must start with K, A, and S, respectively. In the last two sessions, they are asked to generate words belonging to the categories of animals and fruits.[16]

Geriatric depression scale

The Geriatric Depression Scale (GDS) is a self-report yes/no questionnaire to identify depression symptoms in the elderly.[17]

Visit 1

After administration of cognitive function tests, patients were trained using a placebo Diskus device. The training was provided by the same researcher, following the steps described in the Guide to Aerosol Therapy Devices [Table 1].[18] Inhaler technique steps were first verbally instructed, and then practically shown. Afterward, each patient was asked to describe these steps verbally, and repeat them after correction of any misunderstandings. This procedure was repeated until the patient described all steps correctly. It was followed by evaluation of the performance on the inhaler use. Patients were asked to use the Diskus device, and the performance test was repeated until they achieved three consecutive error-free trials. The use of three consecutive error-free trials is a common benchmark for training and usability testing, and this criterion was used in similar studies.[19]

We recorded the time from the incorrect performance during both verbal and practical training steps to the three consecutive error-free trials. At the end of the training, patients were asked to rate the practicability of the Diskus device on a 0–10 visual analog scale (0: very difficult to use and 10 very easy-to-use).

Visit 2

One week after Visit 1, each patient was asked to demonstrate how they used the Diskus device as taught during Visit 1 without any reminder or demonstration. Patient's inhalation technique was scored as effective or ineffective. Mistakes made in steps 1, 2, 4, 5, and 6 in Table 1 were considered major errors, and mistakes made in other steps were considered minor errors. One major error or two minor errors were evaluated as ineffective usage of Diskus device. However, it was classified as effective if there was no error or one minor error unlikely to affect the dose the patient was receiving.

Statistical analyses

The cognitive test scores obtained by participants were compared to the data from a larger sample group of COPD,[20] and transformed into a Z value. The higher the Z score the better the cognitive function of the participant. The relationship between cognitive tests and parameters for learning how to use a Diskus device was calculated using the Pearson's correlation coefficient. Group differences were compared with one-way analysis of variance) for normally distributed-dependent variables (DVs), with Mann–Whitney U-tests for nonnormal DVs, and with Chi-square tests for categorical variables. The level of statistical significance was set at $P < 0.05$.

Results

Twenty-nine inhaler-näive patients completed the study. The demographic and clinical characteristics of participants are shown in Table 2. The mean age of participants was 56.8 years. The mean FEV_1 was 65.4% of the predicted value.

Table 1: The technique for use of Diskus device by steps

Open the device
Slide the lever from left to right
Breathe out normally; do not exhale into the device
Place the mouthpiece into the mouth and close lips tightly around the mouthpiece
Keep device horizontal while inhaling dose with a rapid and steady flow
Remove the mouthpiece from the mouth and hold breath for 10 s or as long as comfortable
Be sure not to exhale into the device
Store the device in a cool dry place
Observe the counter for the number of doses remaining and replace when appropriate

Table 2: Demographic and clinical characteristics of patients with chronic obstructive pulmonary disease

Age (year)	56.8 (10.1) 40-80
Smoking, packs/year	33.9 (9.4) 20-50
BMI, kg/m^2	27.1 (6.3) 18.3-43.1
Education, year	5.9 (2.3) 3-15
FEV_1, percent predicted	65.4 (20.3) 26-106
Geriatric depression score	7.7 (4.2) 0-16
Ease of use rating (VAS score)	8.2 (1.6) 5-10
Cognitive tests	
MMSE	25.4 (2.9) 17-30
Trail making A + B	204 (73.6) 55-320
Clock drawing	3.7 (0.7) 2-4
Forward span	6.9 (2.1) 4-13
Backward span	3.7 (1.2) 2–7
Brown-Peterson	39.9 (6.9) 23–53
Verbal fluency	44.8 (13.6) 23–78
GOLD categories (*n*)	
A	15
B	7
C	2
D	3

Mean (SD) minimum-maximum values are reported. (*n*=29). FEV_1: Forced expiratory volume in 1 s, MMSE: Mini-mental state examination, GOLD: Global initiative for chronic obstructive lung disease, VAS: Visual analog scale, SD: Standard deviation

During the training session (Visit 1), participants described the steps to use a Diskus device verbally. The verbal training continued until they could describe them without an error. Participants completed verbal training with an average error of 1.3 (min = 0 and max = 3). Then, they used the device by themselves until they were able to use the device 3 times consecutively without making an error. The average number of errors during the practice was 1.6 (min = 0 and max = 4), which was significantly larger than 0 ($P < 0.001$). Participants completed training session in 10.3 min on average (min = 4.9 and max = 18.3).

We investigated the association between training session performance and cognitive scores of participants [Table 3]. We observed several significant correlations. There was a significant negative correlation between MMSE, which measures general cognitive decline, and performance during practice session. As the global cognitive scores of the participants (MMSE scores) decreased, number of errors and time-to-complete, the training session were increased. There was a significant correlation between trail making test A+B and training session performance. An increase in the trail making A+B test score is related with deficits in psychomotor coordination, attention, planning, or working-memory processes. All of these processes are associated with the ability to use a Diskus device. There was a significant correlation between working memory assessments (Backward Span and Brown–Peterson test) and practice session performance. Working memory is related with the ability to hold information in mind in the face of distractors. As the working memory score decreased, the training session performance deteriorated.

We calculated the average percentage of errors for each step separately [Figure 1]. Percentage of errors was distributed similarly across errors for the verbal and practical performance. The errors were higher at the second (verbal 17.7% and practical 20.2%), fifth (verbal 13.9% and practical 20.2%), and ninth (verbal 20.3% and practical 16.3%) steps.

During the test session (Visit 2), participants' use of a Diskus device was evaluated. Seven out of 29 patients were failed to use the device correctly. Patients who failed to use the device had higher number of practical errors in the training session ($P < 0.05$), and it took longer for them to complete the training session ($P < 0.01$). Interestingly, patients who failed to use the device correctly had given higher easy-to-use ratings to the device at the end of the training session ($P < 0.01$). We also compared cognitive scores of patients who could and could not use the device. We found that MMSE, trail making test A+B, clock drawing, and total Z scores were significantly different between these two patient groups [Table 4].

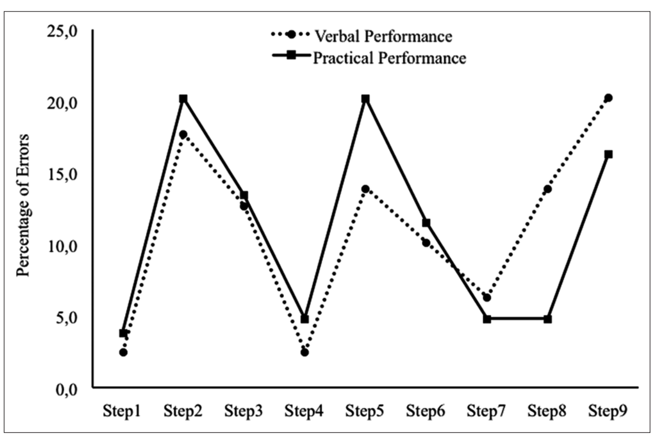

Figure 1: Percentage of verbal and practical errors as a function of Diskus device usage steps in the first visit

Discussion

Our results have shown that parameters indicating the ability to learn how to use a Diskus DPI device in patients with COPD such as description of device use, correct use of the device in the shortest period are associated with cognitive functions of the patients. Patients' effective use of a Diskus device 1 week after the training is associated both with practical skills during initial learning and cognitive functions. Therefore, we found that patients with poor cognitive functions had more difficulty in learning how to use a Diskus device, and patients with poor practical performance in the long term had a poorer cognitive function.

The benefits of using cognitive screening tests for determining which patients could properly use inhalation medications were first shown using MDI medications.[7,21] Allen and Prior found a strong relationship between an abbreviated mental test score of <7/10 and inadequate technique.[21] Another study showed a relation between an MMSE score, also used in our study, of <24/30 and incompetent MDI technique.[7]

Table 3: The correlation between cognitive test *Z*-scores and practice session performance

	Verbal errors	Practical errors	TCTT
MMSE	−0.38*	−0.59**	−0.54**
Trail making A + B	0.48**	0.47*	0.58**
Clock drawing	−0.34	−0.08	−0.29
Forward span	−0.24	−0.24	−0.18
Backward span	−0.36	−0.52**	−0.42*
Brown-Peterson	−0.29	−0.32	−0.43*
Verbal fluency	−0.20	−0.23	−0.28
Total cognitive score	−0.33	−0.39	−0.37

*P<0.05, **P<0.01. (n=29). MMSE: Mini-mental state examination, TCTT: Time to complete three consecutive error-free trials

Table 4: The median scores of patients who could or could not use the Diskus device correctly in Visit 2

	Correct (n=22)	Incorrect (n=7)	*P*
Number of verbal errors	2.0	2.0	NS
Number of practical errors	2.0	3.0	0.05
Diskus performance test time (s)	128	302	0.001
Easy-to-use rating	8.0	10.0	0.01
MMSE (*Z*-score)	0.3	−0.6	0.01
Trail making A + B (*Z*-score)	−0.1	0.7	0.01
Clock drawing (*Z*-score)	0.5	−0.5	0.05
Forward span (*Z*-score)	−0.1	−0.5	NS
Backward span (*Z*-score)	0.1	−0.7	NS
Brown-Peterson (*Z*-score)	0.4	−0.3	0.05
Verbal fluency (*Z*-score)	0.0	−0.8	NS
Total cognitive score (*Z*-score)	0.2	−1.1	NS
Geriatric depression symptoms	8.5	9.0	NS
Age (years)	53.5	59.0	NS
Education (years)	5.0	5.0	NS

MMSE: Mini mental state examination, NS: Not significant

It has been suggested that not all patients with normal cognitive functions would be able to use inhaled medications.[3] In the present study, we observed that scores of the Brown–Peterson and trail making tests A+B, which assess higher-order cognitive functions other than global cognitive functions were associated with performance on the use of inhaler device during both first and second visits.

Following the MDI medications, alternative inhaler devices have been developed since 1990s, and they require fewer operational steps and less coordination; thus, they are easy-to-use. In general, cognitive screening tests have worked in these medications as well with respect to the assessment of usability with appropriate technique.[3,22,23] Similar to our study, Fraser *et al.* studied the relationship between the ability to use a Diskus device and cognitive functions.[24] They found that the ability to use a Diskus device was higher in patients with a higher MMSE performance. Unlike our study, participants of this study were residents of nursing facilities, and in the advanced age (86 ± 9 years) group. In the present study, our population may reflect daily clinical practice much better since they were selected among patients presenting to the outpatient center, who had a mean age of 56.8 ± 10.1 years. Similarly, Fraser *et al.* showed that 95% of patients were able to use the Diskus device properly after training; however, their long-term performance outcomes are unknown. Other studies have shown that incorrect inhaler use is possible even in a short period after initial training.[9,19]

In a study investigating which factors determined handling errors in DPI use, Wieshammer and Dreyhaupt showed that patients who received training on Diskus experienced less essential errors than those who did not receive any training.[4] On the other hand, even patients who received training showed 23.1% essential errors in DPI use. Although our patients received a comprehensive training on inhalers and the training was terminated after all patients achieved proper use of the device, 7/29 (24.1%) patients had ineffective technique during the control visit after 1 week. It suggests that training on inhalers provided at the beginning of treatment would not ensure consistently proper use of the device by the patient.

In a study evaluating the usability of different DPIs using cognitive ergonomics, Franks *et al.* found that the most critical error was "not pushing the lever back to load the inhaler with medication."[19] It was also one of the most critical errors made during both verbal and practical performance evaluation of the Diskus training in our study. In a review by Allen, the steps where most of the errors were made were similar to the steps with most common errors observed in our study.[3] The main difficulties included problems with sequencing, coordination, and dexterity. In support of his findings, we found that the performance in the trail making test A+B was associated with the ability to use the device both during Visit 1 and Visit 2. The trail making test A+B focuses on deficits in psychomotor coordination, attention, planning, or working-memory processes.[13]

In a recently published study, we found an independent relationship between the number of exacerbations during previous year and cognitive functions in COPD patients.[20] However, the design of the study did not allow us to reveal a causal link between these two variables, i.e., it did not provide any answer to the question if cognitive functions were reduced as a result of exacerbations in patients with exacerbations or those with poor cognitive functions experienced frequent exacerbations as a result of poor self-care. The present study suggests that poor cognitive functions have a negative effect on the ability to learn how to use an inhaler. It has been already shown that improper use of inhalers has detrimental consequences for clinical efficacy in patients with COPD.[25] These results suggest that poor cognitive functions in patients with COPD may lead to a poor inhaler performance and higher exacerbation rates.

Similar to the study by Franks *et al*. our patients rated inhalers as easy-to-use.[19] It is also noteworthy that the ineffective group of patients had higher easy-to-use ratings for the Diskus device when effective and ineffective groups in use of inhalers were compared during their second visit. In addition, the comparison between effective and ineffective groups in use of inhalers was compared during their second visit showed no difference in the verbal test while errors in the practical test were higher in the ineffective group. These results indicate that physicians should check their patients' use of inhaler devices through regular monitoring rather than verbal feedbacks.

Molimard *et al*. found a critical error of 12% in the Diskus device. In our study, this rate was higher (24%).[26] However, their study included higher number of patients (896) who used a Diskus device compared to our study. The smaller number of the population including inhaler naïve patients was a limitation of the present study. Another limitation was a visual evaluation of inhalation efforts during inhaler use of our patients. In case of any inadequate inhalation efforts, measurement of peak inspiratory flow is recommended.[4] Evaluation of inhalation efforts by objective tests would have provided more accurate results.

Conclusions

We found that cognitive functions are closely associated with the ability to learn and use a Diskus device in COPD patients. Considering cognitive functions from the first diagnosis in these patients, patients with a poor performance of Diskus use can be identified earlier, and their management may be improved by selecting alternative methods of administration.

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Conflicts of interest
There are no conflicts of interest.

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