ORIGINAL RESEARCH

Inhaler Operability and Patient Satisfaction Regarding Genuair[®] and Respimat[®] Inhalers for Chronic Obstructive Pulmonary Disease: A Randomized Crossover Study

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ABSTRACT

Introduction: Tiotropium via the Respimat[®] device, once daily, is a common treatment for patients with chronic obstructive pulmonary disease (COPD). Acclidinium via the Genuair[®] device, twice daily, is an alternative option. However, there are few studies comparing the two devices. We evaluated inhaler operability, patient satisfaction, and patient preference between Genuair and Respimat inhalers after 2 weeks of daily use.

Methods: COPD patients were randomly assigned to a Genuair or Respimat treatment group at Week 0, and were switched to the other treatment at the end of Week 2. The primary endpoint was the correct operation rate of the devices. The secondary endpoints included number of instructions needed to correctly operate the devices, number of technique

errors, overall patient satisfaction, and willingness to continue using a device.

Results: Fifty-four outpatients (mean age 74.3 ± 10.1 years, 52 men) were enrolled, and all completed the study. The correct operation rate for the Genuair device was significantly higher than for the Respimat device ($96.0 \pm 7.4\%$ and $89.1 \pm 12.8\%$, respectively; $p < 0.001$). Patients required significantly less instruction to handle the Genuair device correctly and made fewer technique errors compared to the Respimat device. The mean overall satisfaction scores were significantly better for Genuair than Respimat, and significantly more patients were willing to continue using the Genuair device.

Conclusion: Our findings suggest that the Genuair device is suitable for COPD patients, especially for those who are less adherent to treatment because of difficulties in inhaler handling, compared with the Respimat device.

Trial Registration: Clinical Trials Registry (R000022399, UMIN000019373, 23/October/2015).

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Keywords: Chronic obstructive pulmonary disease; Genuair[®]; Inhalation device; Inhaler operability; Patient satisfaction; Questionnaire; Respimat[®]

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INTRODUCTION

Inhaled medications now play a pivotal role in the treatment of chronic obstructive pulmonary disease (COPD). Major therapeutic guidelines for COPD, including the GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines, recommend long-acting inhaled bronchodilators for the first-line treatment of COPD [1, 2]. Inhaled medications containing long-acting muscarinic antagonists (LAMA), long-acting beta 2 agonists (LABA), or a combination of both are used in daily clinical practice world-wide. However, patient adherence to inhalation drugs is generally poorer than to oral medications [3] or combination drugs [4]. Inhalation adherence is a significant factor in the management of COPD. Besides comorbidities and disease severity, compliance with treatment was identified as the most notable risk factor for COPD exacerbation, increased mortality, health-care cost, and hospitalization [5, 6]. It was considered that the operability, patient satisfaction, and preference for devices were very important factors with respect to COPD treatment efficacy.

Acclidinium bromide (Almirall, SA, Barcelona, Spain) is a LAMA that is administered via a Genuair® device (also marketed as Pressair®), a breath-actuated dry-powder inhaler with multiple patient feedback mechanisms to confirm proper use of the inhaler.

Beier et al. investigated inhaler preference through a double-blind, double-dummy, randomized, multicenter, placebo- and active-controlled study comparing 400 µg acclidinium administered via Genuair BID to 18 µg tiotropium administered via a HandiHaler® device daily over a 6-week period in patients with moderate to severe COPD [7]. At the end of the 6-week period, significantly more patients preferred Genuair to HandiHaler (80.1% and 10.7%, respectively, $p < 0.0001$), with few patients having no preference for either inhaler (9.2%). Approximately 80% of patients answered that the Genuair device was preferable in terms of ease of use, convenience, ease of learning, ease of holding, ease of operation, ease of dose preparation, and user feedback. When

assessing patient willingness to continue with a device, more patients were willing to continue with Genuair than HandiHaler, as indicated by a higher mean rating in the preference scale at week 6 (88.8 vs 45.4, $p < 0.0001$) [7]. An open-label, randomized, crossover study by van der Palen et al. also compared patient preference, satisfaction, and the number of errors related to inhaler use between the Genuair and HandiHaler in patients with moderate to severe COPD [8]. Overall, more patients were significantly more satisfied with and preferred Genuair to HandiHaler (79.1% vs 20.9%, $p < 0.0001$). When comparing the number of errors between the two inhaler devices, seven patients experienced an error with the Genuair device compared with 19 patients with the HandiHaler device (6.7% vs 18.1%, $p < 0.01$). A phase IIb trial comparing acclidinium 100, 200, and 400 µg BID via Genuair to placebo, and formoterol 12 µg BID via the Foradil Aerolizer® (Novartis AG, Basel, Switzerland) device showed that more patients demonstrated a preference for Genuair (75.6% vs 10.3%) and found the inhaler easier to use [9].

The Respimat® Soft Mist™ (Respimat) is a new device introduced to solve the disadvantages of metered dose inhalers and dry powder inhalers. Tiotropium via Respimat (5 µg once daily) improved lung function, health-related quality of life, decreased COPD exacerbations, and was at least as effective as tiotropium via HandiHaler [10, 11]. The TIOtropium Safety and Performance In Respimat (TIOSPIR™) study demonstrated that tiotropium via Respimat (5 µg once daily) was not inferior to tiotropium via HandiHaler in terms of all-cause mortality, and the risk of cardiovascular mortality or major adverse cardiovascular events did not significantly differ between the two treatment periods [12]. Respimat is now an option among the various inhalation devices and is available world-wide, including Japan, for the treatment of COPD. However, there are few studies comparing the Genuair and Respimat devices. In this study, we compared inhaler operability, patient satisfaction, and preference between Genuair and Respimat devices in Japanese patients with COPD.

METHODS

Statement of Ethics Compliance

This was a randomized, cross-over study that was approved by the research ethics committee of the Clinical Research Tokyo Hospital (Shinjuku, Tokyo, Japan), (Approval No. 151022001). The study protocol was registered in the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (R000022399, UMIN000019373, 23/October/2015) before the start of the study. The study was conducted in compliance with the ethical principles of the Declaration of Helsinki (as revised in October 2013), and the Ethical Guidelines for Clinical Research (1/April/2014) issued by the Ministry of Health, Labor and Welfare and the Ministry of Education, Culture, Sports, Science and Technology. Ethical principles, selection of study sites, storing of documents, monitoring, and audit were conducted based on the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)'s Good Clinical Practice guidelines. Written consent was obtained from all patients before the run-in period. Candidate patients received a detailed explanation of the study protocols before providing consent.

The contract research organization performed both data management and monitoring during the study periods.

Patients

The diagnosis of COPD was defined as a post-bronchodilator forced expiratory volume at 1 s/forced vital capacity (FEV1/FVC) rate less than 70% within the past 3 months. Outpatients with COPD who met the following inclusion criteria were enrolled in this study: (1) over the age of 40 and with a smoking history of more than 10 packs a year (smokers or ex-smokers); (2) first usage of both Respimat and Genuair devices; (3) retained sufficient finger function to handle both inhalation devices; and (4) retained the mental capacity to use both inhalation devices. The exclusion

criteria comprised the following: (1) concomitant with bronchial asthma; (2) serious comorbidities, such as respiratory, heart, gastrointestinal, urinary, blood, and kidney disorders; (3) physically unable to handle both inhalation devices adequately, according to the judgment of the respiratory specialists; (4) dementia or other mental conditions that would preclude adequate use of the inhalation devices; (5) contraindications to anti-cholinergic agents; (6) history of adverse responses to anti-cholinergic agents; (7) cancer complications and history within 5 years; and (8) history of poor drug compliance or inappropriate patient status according to the judgment of the doctor.

In order to determine the required number of patients, we assumed that the correct operation rate in our study would have similar trends as the device preference rate found in previous studies, and performed the following analysis. A previous study found that the preference rate was 45.6% for Respimat and 17.5% for HandiHaler, or in other words, Respimat was approximately 2.6 times more preferable than HandiHaler [13]. Another study found that the preference was 65.1% for Genuair and 16.6% for HandiHaler [8]. Since Respimat was 2.6 times more preferable than HandiHaler, the preference for Respimat was estimated to be 43% ($16.6\% \times 2.6$). Accordingly, it was assumed that the preference would be 65% for Genuair and 43% for Respimat. We calculated that 50 patients per group were required to obtain at least 80% power at a two-sided significance level of 5% with an estimated standard deviation (SD) of 70%, due to high variability in both groups, and an effect size of 0.6 with an assumed dropout rate of 10%. Since the study was to be conducted in a crossover manner, 50 patients were required in total. The analysis was performed on an intention-to-treat (ITT) population.

Therefore, to account for possible drop-outs, 54 patients with COPD (mean age 74.3 ± 10.1 years, 52 male and 2 female patients) were enrolled from among the outpatients at the Tohno Chou Clinic between October 2015 and December 2015.

Inhalers and Medication

The study design is shown in Fig. 1. Each patient visited the study site having had no inhalation medication via Genuair and Respimat throughout the duration of the disease period. At the first visit (Week 0 of phase I), patients were randomly assigned to receive either 5 µg tiotropium bromide via a Respimat device (one dose per day) or 400 µg aclidinium bromide via a Genuair device (two doses per day, 800 µg total daily), using a permuted block randomization system. There was an equal number of patients in each group. The patients were treated with the respective medications for 2 weeks (phase I, Fig. 1), then switched to the other treatment and treated for another 2 weeks (phase II, Fig. 1).

Assessment Methods

We used the following measures for the evaluation of both devices.

Assessment 1: Correct Operation Rate and Inhalation Technique Errors

At the end of phase I, during the follow-up visit, an instructor checked if the patients were performing each step of the inhalation procedure correctly, calculated the correct operation rate, and also recorded the number of errors in each step of the device inhalation process, using the checklist in Table 2 (items C and D in Fig. 1). The rate of patients who performed the correct operation procedure was calculated for each treatment group. The primary endpoint of the study was a comparison of the average correct operation rate between the Genuair inhaler device and Respimat inhaler device. Assessment 1 and assessment 2 were repeated at the beginning and end of Phase II.

Assessment 2: Required Rounds of Instruction

Before the start of phase I, the patients first received specific training in the inhalation procedures for their assigned device from a trained instructor. The instructor repeated the

Fig. 1 Study design

training and counted the rounds of instruction needed for the patient to correctly perform the procedure. The inhalation procedure for each device consisted of 11 items, which are listed in Table 2 (items A and B in Fig. 1). Correct operation was defined as performing each checklist item with no error.

The details of method were as follows: The inhalation procedure checklists were evaluated by an instructor at weeks 0 and 2. At week 0, the instructor first demonstrated the inhalation procedure, which the patients then tried. The instructor repeated the inhalation procedure until the patients showed complete mastery, and the number of times guidance provided was counted and recorded on the checklist. If patients mastered the inhalation procedure after 3 repetitions of guidance, the instructor checked '3'. When the number was less than 3, that device was considered not difficult to handle, compared with those requiring many guidance repetitions.

Assessment 3: Dyspnea Scale

Patients were asked to complete the modified Medical Research Council dyspnea scale (mMRC) at the start and end of phase I (item E in Fig. 1). However, the mMRC was not administered at the end of phase II, considering the pharmacological influence of the previous medication from phase I.

Assessment 4: Patient Questionnaire

Patient satisfaction and preference were assessed via the following questionnaire at the end of each phase (item F in Fig. 1). The patients scored their responses from 1 to 5, with 1 representing the best response, and 5 the worst.

1. Was it easy to learn how to use the inhaler?
2. Was the inhaler easy to carry around?
3. Was the preparation for inhalation easy?
4. Was it easy to inhale the medication?
5. Did you feel that you inhaled correctly?
6. What is your overall impression of the inhaler?
7. Do you hope to keep using this inhaler?
8. Are you satisfied with the user-friendliness of this inhaler?

Statistical Analysis

The significance level was set at 5%. Data are presented as mean $\pm$ standard deviation. Comparisons of each index in both treatment periods were performed using the Wilcoxon rank sum test and Chi squared test. All statistical analyses were performed using JMP ver. 10 (SAS Institute, Cary, NC, USA).

RESULTS

Patients

Fifty-four outpatients with COPD (mean age 74.3 ± 10.1 years, 52 male and 2 female patients) were enrolled between October 2015 and December 2015. The patients' characteristics are shown in Table 1.

Assessment 1: Required Rounds of Instructions

Twenty-four patients (44.4%) required only one round of instruction to correctly perform the Genuair inhalation procedure, and another 24 (44.4%) required two (Fig. 2). Conversely, only two patients (3.7%) were able to perform a correct inhalation procedure with the Respimat device after one round of instruction, and 29 (53.7%) and 12 patients (22.2%) required two or three rounds, respectively. The average rounds of instruction required was 2.74 ± 1.23 for Respimat versus 1.83 ± 1.28 for Genuair ($p < 0.001$). Using the inhalation procedure checklists in Table 2, we investigated the required number of rounds of instruction to perform each individual step correctly. The average number for each step was lower for Genuair than for Respimat (Table 3).

Assessment 2: Correct Operation Rate and Inhalation Technique Errors

The primary endpoint, correct operation rate, was significantly higher for the Genuair device than for the Respimat device ($96.0 \pm 7.4\%$ and $89.1 \pm 12.8\%$, respectively; $p < 0.001$) (Fig. 3).

Table 1 Patient characteristics

	<i>N</i>	(%)
Gender		
Male	52	(96.2)
Female	2	(3.7)
Disease type		
Emphysema type	44	(81.4)
Non-emphysema type	10	(18.5)
Severity		
1 stage	10	(18.5)
2 stage	25	(46.2)
3 stage	12	(22.2)
4 stage	7	(12.9)
Smoking status		
No	45	(83.3)
Yes	9	(16.6)
COPD treatment before enrollment		
LAMA	9	(16.7)
LABA	10	(18.5)
LABA/LAMA	7	(13.0)
Theophylline	14	(25.9)
ICS	0	(0.0)
ICS/LABA	21	(38.9)
Non-pharmacological therapy		
No	46	(85.2)
Yes	8	(14.8)
Concomitant medication		
No	37	(68.5)
Yes	17	(31.5)
	Mean	±SD
Age (years)	74.3	±10.1
Height (cm)	161	±6
Weight (kg)	58.4	±10.1
BMI (kg/m ²)	22.4	±2.1
Disease duration (years)	3.8	±4.1
Respiratory function test		
FEV ₁ (L)	4.36	±20.8
FVC (L)	2.68	±0.76
FEV ₁ % (%)	55.5	±13.7
%FEV ₁ (%)	61.6	±22.3

Table 1 continued

	Mean	±SD
IC (L)	2.07	±0.61
MMF (L)	0.76	±0.38
V25 (L/S)	0.29	±0.13
V50 (L/S)	1.04	±0.66
Respiratory inspiratory flow rate (L/min)	139	±52
mMRC responses		
Genuair [*]	1.74	±1.10
Respimat [*]	1.81	±1.27
Smoking duration (years)	40.4	±14.0
Number of cigarettes smoked (number/day)	27.3	±12.1

^{*} *n* = 27 (evaluated at phase I)

FEV₁ forced expiratory volume in one second, FVC forced vital capacity, %FEV₁ percent predicted forced expiratory volume in one second, MMF maximal mid-expiratory flow rate, SD standard deviation

The average number of inhalation technique errors was significantly lower for the Genuair device than the Respimat device (0.44 ± 0.80 and 1.28 ± 1.53 , respectively; $p < 0.001$) (Fig. 4). A detailed breakdown of the error rate for each individual step is shown in Fig. 5.

Assessment 3: Dyspnea Scale

There were no significant differences between the responses of patients from the Genuair and Respimat treatment groups at the beginning of phase I (1.74 ± 1.10 vs 1.81 ± 1.27 , respectively, $p = 0.929$), or at the end of phase I (1.78 ± 1.05 vs 1.48 ± 1.15 , respectively, $p = 0.316$) (Table 1).

Assessment 4: Patient Questionnaire

The results of the patient questionnaire are summarized in Table 4. The Genuair device was rated significantly better in all the measured aspects, except “was the inhaler easy to carry around?”, where there was no significant difference between the two devices (Genuair vs Respimat, 2.78 ± 0.41 vs 2.89 ± 0.37 , respectively, $p = 0.155$). The mean score for the

Fig. 2 Number of rounds of instruction needed to correctly perform the entire inhalation procedure. Instructions were performed at the start of each phase. *Dark gray*

bars represent Genuair; *light gray bars* represent Respimat. Data are presented as mean $\pm$ SD

Genuair device (2.24 ± 0.41) was significantly better than for the Respimat device (2.61 ± 0.48 , $p < 0.001$).

Evaluation of Safety (Adverse Events)

No serious adverse events were reported over the course of both treatment periods.

DISCUSSION

In this randomized cross-over study, we compared the correct operation rates, errors in inhaler technique, and patient satisfaction and preference between Genuair and Respimat inhalers in patients with COPD. Patients using the Genuair devices required significantly less instruction, and retained that knowledge better after two weeks (significantly higher correct operation rate and fewer errors). A previous study found that significantly fewer patients experienced a critical error, defined as an error affecting drug delivery, with the Genuair device compared to the HandiHaler device (2.9% vs 19%, respectively, $p < 0.0001$) [8]. These results suggest that the Genuair device is generally well tolerated in patients with COPD, and there were fewer errors affecting drug delivery than in both tiotropium devices.

As shown in Table 2, the handling of the inhalation devices is divided into three stages: before, during, and after inhalation. Although

the number of steps in each stage differed between the devices, patients generally required less instruction before they were able to handle the Genuair device, across all stages (Table 3). There are six checklist items regarding the handling procedure before inhalation in the Respimat device, compared to just four in the Genuair device. Not only are there more steps required before inhalation, but they appear to be more complex and harder to grasp. Furthermore, the occurrence of technical errors in checklist items No. 1 and No. 4 were remarkably more frequent in the Respimat device, compared to fewer technical errors before inhalation in the Genuair device (Fig. 5). Conversely, there are five checklist items regarding the handling procedure during inhalation in the Genuair device, compared to three in the Respimat device (Table 2). Nevertheless, the required rounds of instruction in each step in this stage were actually greater in the Respimat device than in the Genuair device (Table 3). This suggests that the three steps during inhalation in the Respimat device may be more difficult and time-consuming for some patients. Figure 5 shows that there were a greater number of technique errors during inhalation in the Respimat device, compared to the Genuair device. The responses to the patient questionnaire were consistent with the above results (Table 4). The majority of errors with the Genuair device occurred in step No. 1 and 4, before inhalation, and step No. 7 and 8, during inhalation. These findings were consistent with

Table 2 Checklist of inhalation procedures for each device

Genuair inhalation procedure checklist

Before inhalation

- (1) Device held correctly (Inhaler held horizontally)
- (2) Mouth cap removed
- (3) Button pushed correctly until inhaler sign turns green
- (4) Button released correctly

During inhalation

- (5) Does not blow into inhaler after the dose is loaded
- (6) Inhales with device kept horizontally
- (7) Inhales powerfully till the sign turned from green to red and a click sound is heard
- (8) Inhales the prepared dose thoroughly
- (9) Seal the lips around the mouthpiece during the inhalation with Mouth corners closed

After inhalation

- (10) Breath held for a sufficient time
- (11) Cap is replaced with no extra manipulation after inhalation

Respimat inhalation procedure checklist

Before inhalation

- (1) Rotates the inhaler with the mouth cap facing upwards
- (2) Turns the transparent case 180 degrees until it clicks into place
- (3) No unnecessary spray by placing case back earlier or by rotating halfway
- (4) Does not rotate the inhaler looking in the spray nozzle with the cap open
- (5) Does not rotate the inhaler with the spray button pushed down
- (6) Does not open the cap in the wrong direction before inhalation

During inhalation

- (7) Able to breathe along with the drug spray
- (8) Direction of the drug spray stable
- (9) Inhales slowly and deeply

After inhalation

- (10) Able to hold breath for several seconds immediately following inhalation
- (11) Cap is replaced with no extra manipulation after inhalation

the results of a previous study [8]. Overall, there were significantly more errors in technique with Respimat than with Genuair (1.28 ± 1.53 vs 0.44 ± 0.80 times, respectively, $p < 0.001$)

(Fig. 4), which may have led to the higher patient satisfaction with and preference for the Genuair device, as demonstrated in the patient questionnaires. A recent study also showed that

Table 3 Required rounds of instruction to correctly perform each step of the inhalation procedure at the start of each phase

Genuair										
Before inhalation			During inhalation				After inhalation			
No.1	No.2	No.3	No.4	No.5	No.6	No.7	No.8	No.9	No.10	No.11
1.11 ± 0.32	1.07 ± 0.33	1.09 ± 0.29	1.30 ± 0.50	1.00 ± 0.00	1.07 ± 0.26	1.65 ± 1.32	1.33 ± 1.08	1.00 ± 0.00	1.04 ± 0.19	1.00 ± 0.00
Respimat										
Before inhalation			During inhalation				After inhalation			
No.1	No.2	No.3	No.4	No.5	No.6	No.7	No.8	No.9	No.10	No.11
1.30 ± 0.77	1.63 ± 1.12	1.78 ± 1.22	1.74 ± 1.23	1.32 ± 0.67	2.02 ± 0.94	1.93 ± 1.39	1.83 ± 1.38	1.48 ± 0.97	1.28 ± 0.71	1.06 ± 0.23

the Genuair device was well-accepted and easy to use in a representative sample of the Italian population aged more than 65 years old. [14].

We did not distinguish errors in technique between “critical” and “not critical.” One of the reasons is that handling of each device in the inhalation procedure differs between Genuair and Respimat, because of differences in their structure. Therefore, a procedure that can be critical to the effect of inhaled drug for one device might not be critical for the other device. Therefore, direct comparison of the inhalation procedures between the two devices is difficult. Another reason is that some errors might cause a critical problem in some patients, but might not in other patients. Thus, the investigators did not distinguish between critical and noncritical errors. There were no significant differences in the mMRC scores between the treatment groups in this study. Both drugs have been shown to be effective in large scale clinical trials [15, 16], and the efficacy of the drugs demonstrated in this study was consistent with the previous findings.

One issue associated with the Genuair device is that aclidinium has to be inhaled twice daily, compared to the majority of newly commercialized inhalation drugs, which only require one daily dose. We speculated that this might have a negative effect on patient satisfaction regarding the Genuair device. However, the responses to items 6–8 in the patient questionnaire demonstrate that this was not the case. We did not include a question regarding the difference between once daily and twice daily administration. Though the number of inhalations/day was an important factor that affects adherence in inhalation therapy, the aim of this study was to evaluate the technical errors that sometimes occur in the process of a single inhalation. Therefore, evaluating effects of the number of inhalations was not an aim of this study. A different study assessing the degree of adherence for two standard regimens (i.e. once-daily medication vs. twice-daily medication) had been conducted previously, in which authors did not find any evidence that twice-daily medication is associated with lower adherence [17]. These findings suggest that the traditional therapeutic method of twice daily inhalations should still be considered.

Fig. 3 Correct operation rates for each step of the inhalation procedure checklist. This assessment was performed at the end of each phase. *Dark gray bars* represent Genuair; *light gray bars* represent Respimat. *Asterisk:* Wilcoxon rank sum test for mean and standard deviation from No.1 to No.11

Fig. 4 Number of technique errors throughout the whole inhalation process, assessed at the end of each phase. *Dark gray bars* represent Genuair; *light gray bars* represent Respimat

Fig. 5 Error rates for each individual step (Table 2), assessed at the end of each phase

This study had a few limitations. First, the 11-item checklists for each device (Table 2) were created specifically for this study, and have not

been externally validated yet. However, there are currently no other adequate, validated checklists concerning the accurate handling

Table 4 Responses to patient questionnaires

Question	Responses from Genuair treatment group	Responses from Respimat treatment group	<i>p</i> value*
Was it easy to learn?	1.91 ± 0.56	2.22 ± 0.74	0.008
Was it easy to carry?	2.78 ± 0.41	2.89 ± 0.37	0.155
Was preparation easy?	1.87 ± 0.43	2.30 ± 0.63	<0.001
Was inhalation easy?	2.18 ± 0.70	2.69 ± 0.86	<0.001
Did you feel that you inhaled correctly?	2.04 ± 0.75	2.63 ± 0.81	<0.001
What is your overall impression?	2.35 ± 0.64	2.72 ± 0.76	0.008
Do you hope to keep using this inhaler?	2.46 ± 0.75	2.87 ± 0.75	0.005
Are you satisfied with the user-friendliness?	2.31 ± 0.61	2.59 ± 0.68	0.015
Mean score	2.24 ± 0.41	2.61 ± 0.48	<0.001

Responses were on a scale of 1–5, with 1 representing the best response, and 5 the worst. Data are presented as mean ± standard deviation

* Chi-squared test

procedures of either device. Therefore, we included almost all the imaginable handling processes for each device and devised our own checklist. The preliminary usage of these checklists in our daily clinical practice showed they were well-tolerated and easy to use (data not shown), which encouraged us to use them in this study. Second, the number of items in each stage of the checklist does not match between the devices, because of the remarkable mechanical differences between the Genuair and Respimat devices. Third, this study had a small population and short duration. However, in order to enhance the precision of the study, we used a randomized crossover design and set strict inclusion and exclusion criteria. We excluded the patients who might have difficulty with proper inhaler use, such as patients with body malformations, who were unable to read, or had diseases that might affect coordination.

CONCLUSIONS

In this study, significantly higher correct operation rates, fewer errors in technique, and better

satisfaction and preference were shown for the Genuair device compared with the Respimat device. Although acclidinium via the Genuair device requires a twice daily dose, our findings suggest that it is a good treatment option for COPD patients who are less adherent to treatment because of difficulties in inhaler handling.

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integrity of the data and accuracy of the data analysis.

Disclosures. Hiroyuki Ohbayashi, Sahori Kudo, and Masatake Ishikawa declare no conflicts of interest.

Compliance with Ethics Guidelines. This was a randomized, cross-over study that was approved by the research ethics committee of the Clinical Research Tokyo Hospital (Shinjuku, Tokyo, Japan), (Approval No. 151022001). The study protocol was registered in the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (R000022399, UMIN000019373, 23/October/2015) before the start of the study. The study was conducted in compliance with the ethical principles of the Declaration of Helsinki (as revised in October 2013), and the Ethical Guidelines for Clinical Research (1/April/2014) issued by the Ministry of Health, Labor and Welfare and the Ministry of Education, Culture, Sports, Science and Technology. Ethical principles, selection of study sites, storing of documents, monitoring, and audit were conducted based on the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)'s Good Clinical Practice guidelines. Written consent was obtained from all patients before the run-in period. Candidate patients received a detailed explanation of the study protocols before providing consent.

Data Availability. The datasets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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