Comparison of clinical efficacy and satisfaction of Tiotropium via Respimat® administration with and without a spacer in patient with Chronic Obstructive Pulmonary Disease: A randomized control trial

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ABSTRACT

Objective: This study assessed the delivery of tiotropium via Respimat® in addition to standard care of treatment among chronic obstructive pulmonary disease (COPD) patients. We study the efficacy, clinical outcome of handling inhaler device, rate of exacerbation and frequency of hospital admission of tiotropium via Respimat® with and without the use of a spacer (AeroChamber®).

Methods: Randomised, open-label study of COPD patients which was randomised into two groups: spacer or non-spacer groups using tiotropium via Respimat®. Treatment with their pre-existing inhalers continued. Subjects were assessed at weeks 0, and 8 for forced expiratory volume in 1 second (FEV1), COPD assessment tool (CAT), St. George's Respiratory Questionnaire (SGRQ), and satisfaction questionnaire.

Results: We enrolled 96 subjects: 49 in the spacer group and 47 in the non-spacer group. The mean predicted FEV1 in spacer group was 54.48% at baseline and 57.5l% at week 8: p=0.011. In the non-spacer groups, FEV_1 was 54.48% at baseline and 59.20% with a mean increment of 4.72 in both groups: p=0.002. There were no difference of exacerbation rates and hospital admission between both groups. At baseline, mean CAT score in the spacer group was 14.01 which improved to 9.80 (p<0.001) and 14.01 to 8.80 (p<0.001) in the non-spacer group. SGRQ total score reduced in both groups with mean difference of 3.1 (p<0.001) and 3.7: (p<0.001) at weeks 0 to 8.

Conclusion: There was no difference between exacerbation and hospital admissions between both groups. There was no difference in FEV1, CAT and SQRQ score using Tiotropium via Respimat® with or without a spacer.

KEYWORDS:
COPD, Tiotropium Respimat®, inhaler technique, FEV1, CAT, SGRQ satisfaction and quality of life.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable chronic airflow limitation disease caused by exposure to noxious particles or gases.[1] It is the third leading cause of death globally.[1-3] In Malaysia, COPD is ranked as the fifth most common diagnosis of hospital admissions.[4] In the Asia Pacific region, tobacco smoking and air pollution remain the leading cause of COPD.[5]

The main goal of COPD treatment is to control symptoms and reduce exacerbations. Inhalers are the cornerstone of COPD treatment allowing delivery of the active treatment to the target site. The current inhalation devices are pressurised metered-dose inhalers (pMDIs), dry powder inhalers, and soft mist inhalers (SMIs).[1] Poor inhaler technique is a concern and is associated with an increased risk of exacerbation.[6-8]

The selection of inhaler device should be determined by the patients' disease, clinical setting and inhalation technique.[9] Other parameters to consider include patient's inhalation flow, the aerosol velocity, and the inhaled drug particle size.[10] Physical restrictions including weakness, declining vision, poor hearing, low inspiratory strength and decline in cognitive function can impair the ability to recall the correct inhaler techniques which can affect drug deposition in lung.[11,12]

A particle size between 2 and 5 microns has the greatest potential to be deposited throughout the bronchial tree.[13] Ideally a slow and deep inhalation (30L/min) is required for pMDI followed by breath hold pause of ≥4s and optimally up to 10 second.[13] A slow-moving velocity aerosol, with a smaller drug particle size, has achieved more than 50% total lung deposition and better penetration into the distal airway.[14,15]

For the majority of patients prescribed inhalers, poor respiratory effort, poor coordination and inadequate techniques remain a problem. spacers are able to help overcome patients with poor coordination. Spacers vary according to their volume or size, manufacture and propensity to become electrostatically charged, their mode of interface with the patient, and the presence or absence of valves and feedback device. Spacers allow deceleration of plume and obliterates the need for hand-mouth coordination thus making inhaler use easier and decreasing oropharyngeal deposition.[15,16]

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Tiotropium via Respimat® is a SMI approved as a maintenance bronchodilator in 2007. It delivers treatment via a slow-moving fine liquid aerosol.[11,17] It produces fine and extra-fine particles, resulting in higher deposition in the smaller airways and less oropharynx deposition.[18-20]

Coordination needed for the usage of Respimat® inhaler has not been widely studied. The addition of a spacer to the delivery of tiotropium via Respimat® has not been shown to have additional benefits in a small Japanese study.[21] We aimed to study the efficacy, clinical outcome of handling inhaler device, rate of exacerbation, and frequency of hospital admission of tiotropium via Respimat® with and without the use of a AeroChamber®.

MATERIALS AND METHODS

This was a randomised, open label single centre study of outpatient COPD patients in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) conducted between September 2019 and February 2020. The study was approved by the Research Ethics Committee, Universiti Kebangsaan Malaysia, FF-2019-462. This research was registered with clinical trial number NCT04999930. The sample size calculation was performed by using Power and Sample software version 3.1.2 (Dupont & Plummer, 1997) comparing two proportion of exacerbation among spacer and non-spacer participants. We used the exacerbation rates based on the study by Faikh et al.[22] The total sample size calculated was 120 (60 subjects in each group), allowing 20% dropout rate). The power of the study was designed at level of 80%, at two-sided alpha level of 0.05.

Patients with a physician diagnosis of COPD were recruited prospectively from the outpatient clinic. We included the following patients: age more than 40 years, able to use inhaler medication and perform spirometry and no exacerbations in two months prior to recruitment.

Patients were excluded if they had a history of bronchial asthma or if they had a condition that could influence their ability to participate in the study; for example, if they have craniofacial anomalies, they are unable to perform or are contraindicated to do spirometry. Patients were allowed to continue with their usual inhalers during the study period. Following screening, baseline demographic data including age, gender, body-mass index (BMI), education level and race were recorded. Spirometry was performed by a trained technician using SpiroUSB (CareFusion).

The primary outcome was to compare the frequency of exacerbation and hospital admission using tiotropium via Respimat® with and without a spacer. For the purpose of this study, we use a similar type of spacer (AeroChamber Plus® Flow-Vu®) in our subjects. Secondary outcome was to examine mean difference in FEV1 between the treatment group, to identify and compare inhaler technique error between the group, to assess quality of life (SGRQ and CAT questionnaire) and to assess patient's satisfaction and preference, attitudes, and perceptions about their inhalers.

CAT score questionnaires were used as a tool to quantify patients' overall disease control. It is available in multiple languages depending on patient's preference.[23] In the SGRQ, a mean change score of four units is associated with slightly efficacious treatment, eight units for moderately efficacious change and 12 units for very efficacious treatment.[24] It is a score range from 0 to 100 with a higher score indicating the worse quality of life.

In our study, a COPD exacerbation is defined as a complex of lower respiratory events/symptoms (increase or new onset) related to underlying COPD, with a duration of three days or more requiring a change in treatment where a complex of lower respiratory events/symptoms is defined as at least two of the following: shortness of breath, sputum production, cough, wheezing chest tightness; and required changes in treatment including prescription of an antibiotic or systemic steroid or newly prescribed maintenance respiratory medication (bronchodilator and theophylline).

When performing spirometry, subjects were asked to blow out for at least 6 seconds according to the American Thoracic Society (ATS) criteria. This was performed at least three times and a maximum of eight tests depending on the quality of test. A minimum of three acceptable measurements were recorded for each subject, and the test will only be considered if the variation between the two best readings is less than 5%. The COPD assessment tool (CAT) and St. George's Respiratory Questionnaire (SGRQ) questionnaires were administered in either English, Chinese or Malay language depending on the subject's preference. The inhaler technique was assessed using a checklist documenting the adherence to manufacturers' directions for each inhaler. Patients were asked to demonstrate the use of their inhalers using the actual device. If incorrect technique was observed, the investigator would explain the corrections and ensure proper use.

Eligible subjects were then randomised using simple randomisation using numbered container into two groups: spacer or non-spacer, and both groups were counselled regarding inhaler technique. Patients were instructed that only SPIRIVA® RESPIMAT® was to be used with the AeroChamber®.

At weeks 0, and 8 the following were performed; spirometry to look at the forced expiratory volume in 1 second (FEV_1), COPD assessment tool (CAT), St. George's Respiratory Questionnaire (SGRQ), and satisfaction questionnaire. The satisfaction questionnaire was developed by the authors in a series of meetings. We used framework from Ogasawara et al.,[22] to decide on elements to be included in the questionnaire such as satisfaction level of inhalation with and without a spacer and regarding maintenance of the spacer. In the second phase, a pilot study was carried out to evaluate the feasibility and to modify the questionnaire accordingly.

Assessment of inhaler technique errors and counselling was performed periodically using phone calls. Inquiries regarding exacerbations, side effects and hospitalization if any were also asked during the phone calls.

Table I: Patients demographic and baseline characteristics in aero-chamber and non -aero-chamber group

Demographic variables		Tiotropium Respimat® with aero-chamber (Group A) (n=49) %	Tiotropium Respimat® without aero-chamber (Group B) (n=47) %	p-value
Age (mean±SD), years		73.00±8.76	68.81±9.26	0.110[a]
Body mass index, (mean±SD), kg/m^2		23.70±4.19	25.80±10.00	0.457[b]
Gender	Male	42 (85.7)	42 (89.4)	0.589c
	Female	7 (14.3)	5 (10.6)	
Races	Malay	20 (40.8)	21 (44.7)	0.584[d]
	Chinese	26 (53.1)	21 (44.7)	
	Indian	3 (6.1)	5 (10.6)	
Smoking status	Nonsmoker	9 (18.4)	5 (10.6)	0.361[c]
	Current smoker	7 (14.3)	3 (6.4)	
	Ex-smoker <10 years	15 (30.6)	18 (38.3)	
	Ex-smoker > 10 years	18 (36.7)	21 (44.7)	
Comorbidities	Nil	9 (18.4)	11 (23.4)	0.259[d]
	DM	1 (2.0)	4 (8.5)	
	HPT	22 (44.9)	13 (27.7)	
	DM + HPT	14 (28.6)	10 (21.3)	
	DM + HPT + IHD	1 (2.0)	4 (8.5)	
	HPT + IHD	2 (4.1)	2 (4.3)	
Number of maintenance inhaler	Single	24 (49.0)	19 (40.4)	0.399[c]
	Multiple	25 (51.0)	28 (59.6)	
Duration of COPD	<1 year	7 (14.3)	9 (19.1)	0.667[c]
	1 -5 year	21 (42.9)	16 (34.0)	
	5 - 10 year	14 (28.6)	12 (25.5)	
	> 11 year	7 (14.3)	10 (21.3)	
FEV1 percentage (mean±SD)	55.90±23.03	53.00±20.70	0.519a	
FVC percentage (mean±SD)	61.02±22.31	58.34±18.72	0.686a	
Gold stages	A	0(0)	0 (0)	0.749[c]
	B	22 (44.8)	21 (42.6)	
	C	22 (44.8)	20 (34.0)	
	D	5 (10.4)	6 (12.8)	
CAT score	Low (1-10)	9 (18.4)	13 (27.7)	0.250
	Medium (11-20)	31 (63.3)	31 (66.0)	
	High (21-30)	8 (16.3)	3 (6.4)	
	Very high (>30)	1 (2.0)	0 (0.0)	
mMRC	1	18 (36.7)	15 (31.9)	0.670c
	2	25 (51.0)	28 (59.6)	
	3	6 (12.2)	4 (8.5)	
	4	0 (0)	0 (0)	
SGRQ	Symptom	42.18±17.40	47.32±17.70	0.154[a]
	Activity	44.14±18.74	43.58±19.33	0.887[a]
	Impact	28.43±15.30	30.94±15.21	0.422[a]
	Total	35.63±14.76	37.48±14.32	0.536[a]
Number of exacerbations in the past year	0	33 (67.3)	36 (76.6)	0.771[d]
	1	10 (20.4)	7 (14.9)	
	2	4 (8.2)	3 (6.4)	
	3	2 (4.1)	1 (2.1)	
Number of admissions in the past year	0	48 (98.0)	45 (95.7)	0.613[d]
	1	1 (2.0)	2 (4.3)	
	2	0(0)	0(0)	

[a]Independent t test; [b]Mann Whitney test; [c]Pearson Chi-square; [d]Fisher's Exact test
DM: Diabetes Mellitus, HPT: Hypertension, IHD: Ischemic heart disease

Table II: Exacerbation and hospital admissions during study period of aero-chamber and non -aero-chamber Groups

Variables		Tiotropium Respimat® with Aerochamber n (%)	Tiotropium Respimat® without Aerochamber n (%)	p-value
Exacerbation	Yes	16 (16.7)	11 (11.4)	0.314a
	No	80 (83.3)	85 (88.6)	
Hospital admission	Yes	1 (1.1)	1 (1.1)	>0.950 b
	No	95 (98.9)	95 (98.9)	

[a]Pearson Chi square; [b]Fisher's Exact test

Table III: Comparison of FEV_1, CAT, SGRQ within AeroChamber® group and non-AeroChamber® group and satisfaction between the two groups

Variables	Tiotropium Respimat® with aero-chamber			Tiotropium Respimat® without aero-chamber		
	Before mean (SD)	After mean (SD)	p value	Before mean (SD)	After mean (SD)	p-value
FEV_1	54.48 (21.86)	57.55 (21.03)	0.011	54.48 (21.86)	59.20 (21.09)	0.002
CAT	14.01 (5.13)	9.80 (3.64)	<0.001	14.01 (5.13)	8.80 (3.90)	<0.001
SGRQ Symptom	44.70 (17.64)	34.73 (13.94)	<0.001	44.70 (17.64)	29.04 (15.19)	<0.001
SGRQ activity	43.87 (18.93)	33.34 (14.41)	<0.001	43.87 (18.93)	28.40 (13.53)	<0.001
SGRQ Impact	29.66 (15.23)	20.25 (12.47)	<0.001	29.66 (15.23)	17.14 (11.63)	<0.001
SGRQ Total	36.54 (14.50)	33.77 (108.09)	<0.001	36.54 (14.50)	26.61 (11.41)	0.805
Satisfaction	2.91 (0.18)	3.12 (0.20)	<0.001	3.09 (0.22)	3.25 (0.17)	<0.001

Association of the mean difference at baseline and week 8 between 2 groups

Variables	Tiotropium Respimat® with aerochamber mean difference (SD)	Tiotropium Respimat® without aerochamber mean difference (SD)	p value
FEV_1	-3.07 (11.64)	-4.72 (14.21)	0.3799
CAT	4.21 (3.32)	5.21 (4.03)	0.0621
SGRQ Symptoms	9.96 (16.37)	15.65 (20.44	0.0345*
SGRQ Activity	10.53 (14.65)	15.47 (18.26)	0.0400*
SGRQ Impact	9.41 (14.67)	12.52 (15.75)	0.1585
SGRQ Total	2.77 (2.33)	9.92 (11.93)	<0.0001*
Satisfaction	-0.21 (0.21)	-0.16 (0.19)	<0.0001*

FEV1: Forced expiratory volume in 1s; CAT: COPD assessment test; SGRQ: St George's Respiratory Questionnaire, p-value <0.001 is significant, *Paired T-test

STATISTICAL ANALYSIS

All data were analysed using Statistical Package for Social Sciences (SPSS) version 25.0. The continuous variables were tested with Student t test for normal distribution and Mann-Whitney U test for non-normal distribution to compare between the two groups: spacer and non-spacer. The categorical data were tested with Pearson Chi-square test and Fisher exact test. The results of the data between the two groups were analysed using Independent-sample t-test or its equivalent non-parametric Mann-Whitney U test for parameter non-normal distribution. Paired t-test were used to analysed data in each group. Statistical significance was declared when $p<0.05$.

RESULTS

A total of 137 COPD patients were screened between September 2019 and February 2020. Ninety-six patients fulfilled the inclusion criteria and consented to be involved in the study.

The mean age was 70.95±9.21 years and the majority were men (84, 85.7%). Thirty-nine (40.6%) were current smokers and 33 (34.4%) were lifelong non-smokers. Only 14.6% had no co-morbidities. About 67% of subjects had at least ≥2 comorbidities. More than half the study population had multiple numbers of maintenance inhalers. Nearly half (44.8%) had COPD diagnosis of ≥5 years. Demographic details as well as pulmonary function test results, CAT and SGRQ score were listed in Table I.

There was no association between spacer usage with both exacerbation and hospital admission. During the study period, 16 (16.7%) participants in the spacer group and 11 (11.4%) participants in the non-spacer experienced exacerbations of symptoms (Table II).

The predicted mean percentage FEV_1 was 54.48±21.86%. Majority (77.15) had CAT Score at ≥11. In the past year, 71.9% did not experience any exacerbations and only 3.1% had one hospital admission in the last year.

There was a statistically significant difference between baseline and 8 weeks of treatment in both groups for the following: CAT, SGRQ and satisfaction FEV_1 mean difference of -3.07 in the spacer group and -4.72 in the non-spacer group (Table III). The mean changes in FEV_1 were -1% after 8 weeks of tiotropium via Respimat®.

The mean percentage change in the trough FEV_1 was -3.07% after 8 weeks of treatment in the tiotropium via Respimat® treatment administered with a spacer and -4.72 without a spacer. There was no significant difference in the mean percentage change FEV_1 between tiotropium via Respimat® therapy delivered with and without a spacer (Table III).

There was also no significant difference between tiotropium via Respimat® therapy with and without a spacer with respect to mean percentage difference in CAT score at week 8. However, there was a significant difference in the mean percentage change of SGRQ (symptoms and activity and total) between tiotropium therapy delivered with and without a spacer (Table III).

Inhaler satisfaction scores using tiotropium via Respimat® with and without a spacer at baseline and at 8 weeks are shown in Table IV. At baseline, 47 (49%) subjects had difficulty to assemble tiotropium via Respimat®. The numbers decreased to 22 (22.9%) at week 8. About 67 (69.8%) subjects in the non-spacer group and 33 (34.4%) subjects in with the spacer group found the use of inhaler fairly easy. More than half (61.5%) at baseline and 67.7% at week 8 were not keen to bring along their spacers out of their home (Table IV).

The number of patients who were confident using tiotropium via Respimat® increased from 1 (1%) prior to counselling to 77 (80.2%) at week 8. More than 90% of subjects were

Table IV: Satisfaction of using Tiotropium Respimat® with and without aero-chamber at baseline and at week 8

Questions	Baseline (Week 1)					At Week 8				
	Very n (%)	Fairly n (%)	Somewhat n (%)	Not very n (%)	Hardly at all n (%)	Very n (%)	Fairly n (%)	Somewhat n (%)	Not very n (%)	Hardly at all n (%)
1. How easy was it to assemble the SMI?	2 (2.1)	42 (43.8)	47 (49.0)	5 (5.2)	0 (0.0)	1 (1.0)	72 (75.0)	22 (22.9)	1 (1.0)	0 (0.0)
2. How easy did you find the use SMI?	11 (11.5)	67 (69.8)	18 (18.8)	0 (0.0)	0 (0.0)	3 (3.1)	43 (44.8)	37 (38.5)	13 (13.5)	0 (0.0)
3. How easy did you find the use of SMI with aero-chamber?	1 (1.0)	28 (29.2)	47 (49.0)	19 (19.8)	1 (1.0)	1 (1.0)	33 (34.4)	19 (19.8)	42 (43.8)	1 (1.0)
4. How likely are you to bring along your aero-chamber when you are outside your home?	0 (0.0)	3 (3.1)	59 (61.5)	34 (35.4)	0 (0.0)	0 (0.0)	4 (4.2)	65 (67.7)	27 (28.1)	0 (0.0)
5. How confident are you in using your SMI?	0 (0.0)	1 (1.0)	11 (11.5)	81 (84.4)	3 (3.1)	0 (0.0)	77(80.2)	17(17.7)	2 (2.1)	0 (0.0)
6. After our counselling session, how confident are you now in using your SMI?	1 (1.0)	64(66.7)	30 (31.3)	1 (1.0)	0 (0.0)	51 (53.1)	44 (45.8)	1 (1.0)	0 (0.0)	0 (0.0)
7. How confident are you in maintenance of your aero-chamber?	0 (0.0)	4 (4.2)	90 (93.8)	2 (2.1)	0 (0.0)	0 (0.0)	4 (4.2)	91 (94.8)	1 (1.0)	0 (0.0)
8. Overall, how satisfied are you with the SMI?	0 (0.0)	38 (39.6)	58 (60.4)	0 (0.0)	0 (0.0)	3 (3.1)	75 (78.1)	18 (18.8)	0 (0.0)	0 (0.0)

somewhat confident in the maintenance of AeroChamber® at baseline and week 8. Satisfaction of tiotropium via Respimat® increased from 39.6% to 78.1% after 8 weeks (Table IV).

We assessed inhaler critical errors at baseline and at 8 weeks' treatment. The three common errors of tiotropium via Respimat® in the non-spacer group are : (1) failure to exhale prior to use inhaler - 30 (31.2%); (2) failure to maintain a good seal for 5 breaths after pressing SMI - 29 (30.5%); (3) failure to hold upright with cap close - 17 (17.7%). Common errors of SMI with spacer usage are (1) failure to check the spacer for foreign objects - 35 (36.5%), (2) failure to inhale slowly and deeply - 33 (34.4%), (3) failure to slow down inhalation despite whistling sound - 31 (32.3%).

DISCUSSION

Successful treatment of COPD depends on the effective delivery of bronchodilators to the lungs. Bronchodilators used in stable COPD include SABA, SAMA, LABA and LAMA. Inhalers are the mode of delivery and different inhalers have distinct characteristics which can affect the administration of the drug.

Tiotropium was the first LAMA available for COPD treatment. Tiotropium via Respimat® was approved as a COPD maintenance bronchodilator in 2007 in Europe and in 2014 in the United States and Canada. The use of tiotropium via Respimat® has been shown to increase in FEV_1 and FVC from as early as 24 weeks and reduce both moderate and severe exacerbations.[25,26]

Spacers cause deceleration of aerosol and decrease oropharyngeal deposition as much as 90% and decrease the need for coordination between hand and actuation when used with pMDI. Because of these factors, the use of spacers is established in the treatment paradigms.

While data on the benefit of pMDI and AeroChamber® is well documented, the benefit of the addition of AeroChamber® to the Respimat® device is less studied. To our knowledge, this is the first study in Malaysia to study the benefit of tiotropium inhalation therapy using Respimat®. with the addition of a AeroChamber® in terms of clinical efficacy (FEV1, CAT Score and SGRQ Score), exacerbation and patient satisfaction using inhaler with/out AeroChamber®.

COPD affects mainly males. This is likely related to the smoking habit as smoking causes COPD and it is a predominant male habit. Previous local study done in Malaysia also showed male predominance.[27] In our study, 87. 5% were males and 40% were current smokers.

The majority of patients were in GOLD B (43.7%) and followed by GOLD C (39.5%). We had no patients in Gold A as we are a tertiary referral center. In our study, 17.7% reported one exacerbation in the last 1 year. In terms of symptoms, only 12.5% were highly symptomatic using the CAT score.

We found that the addition of AeroChamber® to tiotropium via Respimat® had no significant improvement in percentage

FEV_1. A small Japanese study involving 20 patients with tiotropium via Respimat® using AeroChamber® and non-AeroChamber® showed similar findings in terms of FEV_1.[21] This may be due to the short duration of both our study (8 weeks) and the Japanese study (2 weeks); as the earliest improvement of FEV_1 was reported at 24 weeks.[25,26]

The COPD assessment tool (CAT) and St. George's Respiratory Questionnaire (SGRQ) were used to assess severity and quality of life. We found improvement in symptoms at the end of 8 weeks of intervention. The mean change in CAT score reduced from 14.01 to 9.80 in the AeroChamber® group and 14.01 to 8.80 in the non-AeroChamber® group. Subjects had regular phone calls and were reminded to use their inhalers and had their technique corrected. This may have contributed to better adherence to the medication.

In the SGRQ scores, there was a statistically significant difference between baseline and 8 weeks of treatment for symptoms, activity, impact, and total score in both groups. The mean change in the domain of symptoms, activity, and impact was more than 12 in the non-AeroChamber® versus AeroChamber® group where the mean change ranged from 9.41 to 9.97. The impact of AeroChamber® appeared to lessen the improvement in the group.
There was no association between the use of AeroChamber® with exacerbations and hospital admission. Twenty-seven patients (27%) had reported exacerbation during the study period. However, we may have missed some symptomatic events as this was based purely on patient's recall. Some subjects may have been reluctant to declare their symptoms accurately to medical staff.

Our study had a lower exacerbation rate compared to other studies. This may be due to our inclusion criteria. Part of the study was conducted during pandemic COVID 19 with strict movement control orders. This may have led to a decrease in infection-related exacerbation.

Inhaler errors affect drug delivery.[28] Studies have shown that inhaler technique errors are common and occur in up to 90% of patients regardless of inhaler device. A real-world study showed that when patients make a single critical inhaler error there is a risk of COPD exacerbation.[29] When invited to demonstrate their tiotropium via Respimat® inhaler technique, at baseline, 100% subjects made ≥1 device use errors.[29] The majority of subjects were unable to ensure a tight seal with lips around the mouthpiece and when mouthpiece was inserted into the AeroChamber®. The other common error was a failure to exhale prior to inhaler use. Device errors in tiotropium via Respimat® have been reported to occur in 6 out of 10 patients. In our study, there was an improvement in the number of errors made at each step of tiotropium via Respimat® at 8 weeks. The number of errors decreased after counselling which was done at baseline and at regular intervals during the 8-week study period.[30]

COPD exacerbations frequently related to poor inhalation techniques potentially impact the quality of life.[12,25] Multiple studies done previously had shown the correlations.[13,25] The decrease in the number of errors translates to a decrease in COPD exacerbations. Our study highlights that in addition to prescribing inhalers, counselling and correction of inhaler technique should also be emphasized in COPD management. This corresponds to one study that showed that without counselling, patients demonstrating correct technique declined by 39% on subsequent visit.[31]

None of our patients had rheumatological comorbidities. Despite that, 49% of subjects had difficulty assembling tiotropium via Respimat® at baseline. Nearly 70% preferred using tiotropium Respimat® without the AeroChamber®. Our patients were using AeroChamber® device at home, but on further questioning, they appeared reluctant to bring the AeroChamber® outside their home citing bulkiness as one of the main reasons. Other studies have also shown a poor uptake of AeroChamber®.[32]

However, we found that with regular counselling, their confidence level to assemble and use SMI improved at week 8 in both groups. Their overall satisfaction using tiotropium Respimat® improved from 39.6% to 78.1%. Other studies have shown that the reported satisfaction rate handling tiotropium Respimat® device from satisfaction rate 63.5-84.3%.[33,34]

Subjects did not find the use of tiotropium Respimat® with AeroChamber® easy. About 49% of subjects found the use of tiotropium Respimat® with AeroChamber® somewhat easy, however at the end of 8 weeks, only 19.8% found it useful. With regards to maintenance of AeroChamber®, less than 5% of subjects were fairly confident. These issues may lead to intentional non-compliance where the patients refrain from using the AeroChamber® or only uses it from time to time.

Our study attempts to mimic real-world use of Spiriva Respimat with AeroChamber®. In our study, subjects were allowed to continue their usual bronchodilators; counselling and reminders were done with a simple phone call. We showed no reduction of efficacy of tiotropium Respimat® with AeroChamber®. The design of our study allowed an accurate short-term recall allowing an accurate representation of patient's satisfaction as each patient experienced the use of tiotropium Respimat® with and without AeroChamber®. These findings suggest that in a subset of patient with poor hand-mouth coordination; AeroChamber® with tiotropium Respimat® is as efficacious in delivering drugs.

This study has several limitations as it is a single-centre study. We did not use the diary to document patient's adherence to AeroChamber®. Therefore, we might have underestimated the true adherence. During the non-intervention period of the study, there were no phone calls and we were unable to monitor and ensure that they were not using AeroChamber®. Phone inquiry was performed on exacerbation which might not be accurate is another limitation of the study.

In our study, the non-AeroChamber® group reported higher satisfaction scores and better quality of life. We conclude that there was no difference of exacerbation and hospital admission between both groups. Tiotropium Respimat® using AeroChamber® does not offer additional benefit in terms of FEV1, CAT and SQRQ score in severe COPD patients. However, we recommend that adding an AeroChamber® to Tiotropium Respimat® may be suitable for a subset of patients with poor and-mouth coordination.

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DISCLOSURE STATEMENT:

The authors declare that they have no competing interests. Appropriate written informed consent was obtained for the publication of this study.

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