

Chronic obstructive pulmonary disease patients' experience using Trelegy as compared with other inhalers

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Introduction: Trelegy is a combination inhaler that is often reported to offer benefits over multiple inhalers. We compared Trelegy use with multiple inhalers for adherence, symptoms, medication beliefs, and medication attitudes.

Methods: This cross-sectional survey of 58 patients compared the patient's experience with Trelegy ($n = 18$) versus any other inhaler ($n = 40$). Outcome variables consisted of Test of the Adherence to Inhalers scale, the Chronic obstructive pulmonary disease Assessment Test (CAT) scale, attitude items from the St. George's Respiratory Questionnaire, the Beliefs about Medicines Questionnaire (BMQ)-necessity subscale, and the BMQ-concerns subscale.

Results: We found that patients using Trelegy had greater CAT symptoms ($M = 19.8$, $SD = 7.75$) in comparison with the any other inhaler group ($M = 15.7$, $SD = 11.10$; $P = 0.04$). We did not find any difference between the groups for adherence or any of the medication attitudes or beliefs. CAT score was positively correlated with the number of months patients were on their current inhaler ($r_s = 0.29$, $P < 0.05$) and their use of a rescue inhaler ($r_s = 0.42$, $P < 0.01$). Patients with more concern about their medications were negatively correlated with the use of a rescue inhaler ($r_s = -0.31$, $P < 0.05$).

Discussion: We found that patients using Trelegy had greater symptoms in comparison with the any other inhaler group, but did not differ for adherence, medication attitudes, or medication beliefs.

Conclusion: We recommend that clinicians should regularly re-evaluate their Trelegy recommendations, as Trelegy use may not be the best therapy for certain patients. Also, a study with a larger sample size can be beneficial to confirm these findings.

Key Words: Nebulizers and vaporizers; medication adherence; chronic obstructive pulmonary disease

INTRODUCTION

There are approximately 328 million people worldwide that have chronic obstructive pulmonary disease (COPD) [1]. COPD is a preventable and treatable disease with inhaler use as the cornerstone of prevention and treatment of COPD respiratory symptom exacerbations [2]. However, patients with COPD may have a limited understanding of their disease and medications, which can lead to poor adherence to their treatment recommendations [3].

For COPD, adherence is an important aspect of inhaler use [4]. Factors that affect inhaler adherence among COPD patients include the number of devices used and the daily dosage frequency; older age and female gender are factors identified with poorer inhaler adherence among COPD patients [5, 6]. In a prospective cohort study among asthmatic patients (which often overlaps with COPD), adherence to inhalers was lower in patients in racial/ethnic minority groups as compared with Caucasian groups [7]. Additionally, environmental exposures (e.g., occupational exposures, tobacco use, and indoor biomass fuel) are more common in low socioeconomic status populations [8]. Furthermore, access to medication and health care is often more limited for patients of lower socioeconomic status [8].

Another major aspect that impacts COPD patients' adherence to inhaler use is their beliefs about the necessity of taking medications and concerns about medication use [9]. The Beliefs about Medicines

Questionnaire (BMQ) assesses a patient's beliefs regarding a specific medication [10]. In a prospective study on beliefs in COPD patients, the BMQ necessity subscale was positively associated with adherence at 3-month and 12-month follow-up, whereas the BMQ concerns subscale was negatively associated with adherence at 3-month and 12-month follow-up [11].

Trelegy is an inhaler that combines three different inhaler medications of fluticasone furoate, umeclidinium, and vilanterol into one inhaler [12]. The manufacturer of Trelegy advertises that the Trelegy inhaler is easy to use, convenient, and that COPD patients are often more adherent to their treatment schedule since it combines three different inhaler therapies into a single device [13]. A study of Trelegy usage compared with the usage of different inhalers with dual therapy of budesonide and formoterol found that the Trelegy group had greater improvement of lung function and fewer symptoms than the dual therapy group [14]. Another study found that Trelegy resulted in less COPD exacerbations and less hospitalizations than the use of either an inhaler consisting of fluticasone furoate and vilanterol or umeclidinium and vilanterol [15]. There is an important research gap for studying whether the potential ease of use for Trelegy is associated with improved adherence. Although Trelegy has potential benefits, it is more expensive than other inhalers. Specifically, a 30-day supply of Trelegy is US\$601.86, whereas prices for levalbuterol range from US\$32.39 to US\$65.21 and

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fluticasone/salmeterol range from US\$89.88 to US\$125.95 [16–18]. Albuterol costs US\$19.05–27.02 per inhaler [19]. To our knowledge, there are no studies comparing Trelegy with multiple inhalers use for adherence, medication beliefs, or medication attitudes. Our study aims to discover whether there is any difference for Trelegy as compared with multiple inhalers use for adherence, symptoms, medication beliefs, and medication attitudes. We hypothesize that Trelegy will have greater adherence than multiple inhalers use.

METHODS

Setting

The study was ethically conducted and received approval from the Nassau Health Care Corporation Institutional Review Board on 29 January 2020. We conducted a survey of patient experience with Trelegy ($n = 18$) versus any other inhaler ($n = 40$) from March 2020 through February 2021 in an outpatient pulmonary clinic in a suburban New York City hospital that typically serves lower income patients. We compared patients taking the Trelegy inhaler with patients taking single or multiple inhalers that comprised of a once-a-day inhaler (inhaled corticosteroid) or additional inhalers of long-acting beta agonist, long-acting muscarinic agonist of all types, including metered-dose inhalers, as well as dry powder inhalers. The inclusion criteria were patients with COPD and were 18 years of age and older. To avoid any bias, all patients that met these criteria were eligible. We recruited patients from a convenience sample of all patients in the clinic. We included all patients who agreed to complete the survey. Surveys were provided in either English or Spanish. Oral informed consent was obtained.

Variables

Demographic variables were age (years), sex (female/male), race/ethnicity (White, African-American, Hispanic), and education level (some elementary school, completed elementary school, some high school, completed high school, some college, completed college). There were three inhaler variables. We used a Likert-style scale to collect respondents' attitudes. It is a psychometric scale to evaluate the views and perspectives towards a brand or product. A Likert-style scale is commonly used in questionnaires. One variable was, "I find it easy to use the inhaler(s) that are prescribed by my doctor". It was measured on a Likert-style scale ranging from 0 = strongly disagree to 4 = strongly agree. Another variable was, "How often do you use your rescue inhaler?" It was measured on a Likert-style scale of 0 = less than once a month, 1 = once a month, 2 = once a week, and 3 = every day. A third variable was, "How many months have you been on your current inhaler(s)?"

Outcome variables

The Test of the Adherence to Inhalers (TAI) scale is a popular measure used for studying inhaler adherence in COPD patients due to its high reliability and validity [20]. It consists of 10 items that ask about how often a patient did not use their inhaler and in which particular situation, for example, when patients are feeling well or on weekend or holiday. A sample item is, "You stop taking your inhalers out of fear of potential side effects". A Likert scale was used to measure all the items ranging from 1 = always to 5 = none/never. All 10 items were added together for a total score. A greater score indicates greater adherence. The items were obtained from a previously published article [20]. The Cronbach alpha reliability test was used to assess the reliability of the test items. It measured 0.82 in our sample. Cronbach's alpha greater than 0.7 refers to a particularly good level.

The COPD Assessment Test (CAT) scale is a popular measure used for studying COPD symptoms because of its high reliability [21]. It consists of eight items that assess degree and symptoms related to breathlessness and its severity in patients with COPD. Items included, "My chest does not feel tight at all" to "My chest feels very tight". A Likert scale was used to measure all the items with a range from 0 = extremely uncharacteristic to 5 = extremely characteristic. All eight items were added together for a total score from 0 to 40. A greater score indicates a greater

impact of symptoms. The items were obtained from a previously published article [22]. Cronbach alpha reliability was 0.90 in our sample.

We used four items from the St. George's Respiratory Questionnaire [23]. The St. George's Respiratory Questionnaire is a popular measure used for evaluating multiple domains related to a patients' respiratory status and well-being and has high reliability and validity [24]. It contains three sections that consisted of frequency and severity of symptoms, activity, and medication impact on the patients. To avoid patient response burden, we chose to only ask four questions from the domain of impact, particularly the patient's attitudes toward taking their medication. A sample item is, "My medication does not help me very much". A dichotomous scale, a case of either one or the other, was used to measure all the items with 0 = False and 1 = True. A higher score indicates more perceived medication limitations. Because of poor Kuder-Richardson 20 reliability of these items, each item was analyzed separately.

Attitudes are important for understanding patient concerns. The BMQ-necessity subscale consisted of five items on how important or necessary it is for the patient to be on their medication. A sample item is, "Without my medicines I would be very ill". A Likert scale was used to measure all the items with a range from 1 = strongly agree to 5 = strongly disagree. All five items were added together for a total score. A greater score indicates patient's stronger beliefs regarding medication necessity. The BMQ-concerns subscale consisted of five items on the patient's worries associated with taking medication, specifically related to worries regarding their inhalers, including the long-term side effects, dependency on their medications, and disruption of life. A sample item is, "Having to take my medicines worries me". A Likert scale was used to measure all the items with a range from 1 = strongly agree to 5 = strongly disagree. All five items were added together for a total score. A greater score indicates patient's greater concern regarding taking their medication. The BMQ items were obtained from a previously published article that reports high reliability and validity [25]. Cronbach alpha reliability in our sample for necessity was 0.78 and for concerns was 0.81.

Statistical analysis

Mean and standard deviation were used to describe the continuous variables. Frequency and percentage were used to describe the categorical variables. Analysis of variance compared the continuous variables with a normal distribution. The Mann-Whitney test compared the skewed continuous variables. The Pearson chi-square test compared the categorical variable of sex. All other categorical variables were compared with the Fisher's exact test due to expected cell size < 5 . The variable of months on current inhaler significantly differed between the inhaler groups and was logarithmic transformed and included as a covariate for the outcome variables. Continuous outcomes were analyzed with analysis of covariance and categorical outcomes were analyzed with logistic regression. Spearman correlation analyses were conducted for the continuous variables. All P values were two-tailed. The significance level was $P < 0.05$. IBM SPSS Statistics version 26 was used for all analyses [26].

RESULTS

Table 1 compares the sample characteristics between the Trelegy and the any other inhaler group. None of the demographic variables of age, sex, and race/ethnicity significantly differed between the Trelegy and the any other inhaler group. The inhaler variable of months on current inhaler significantly differed ($P < 0.05$) where Trelegy had a mean indicating fewer number of months used than the other inhaler group. Ease of inhaler use and how frequency of using a rescue inhaler did not significantly differ between the Trelegy and the any other inhaler group.

Table 2 compares the outcome variables between the Trelegy and the any other inhaler group. The multivariate analysis showed that symptoms as measured by CAT significantly differed between the Trelegy and the any other inhaler group with increased mean symptoms for the Trelegy group ($P < 0.05$). For the other continuous outcome variables of adherence as measured by TAI, BMQ-necessity, and BMQ-concerns, there were no significant differences between the Trelegy and the any other inhaler group. The medication items of "medication does not help

me very much” and “embarrassed using my medication in public” did not significantly differ between the Trelegy and the any other inhaler group. Also, “unpleasant side effects from my medication” and

TABLE 1
Comparisons of sample characteristics

Variable	Any other inhaler (n = 40)	Trelegy (n = 18)	P
Age, years (M, SD)	62.8 (8.96)	66.3 (13.43)	0.25
Sex, male (no., %)	20 (50.0)	12 (66.7)	0.24
Race/ethnicity (no., %)			0.23
White	17 (42.5)	5 (27.8)	
African-American	14 (35.0)	11 (61.1)	
Hispanic	9 (22.5)	2 (11.1)	
Education (no., %)			0.23
Completed college	7 (17.5)	0 (0.0)	
Some college	5 (12.5)	5 (27.8)	
Completed high school	12 (30.0)	6 (33.3)	
Some high school	11 (27.5)	3 (16.7)	
Completed elementary school	2 (5.0)	2 (11.1)	
Some elementary school	3 (7.5)	2 (11.1)	
Inhaler easy to use (M, SD)	3.3 (0.91)	3.2 (1.20)	0.82
Months on current inhaler (M, SD)	35.0 (38.56)	11.5 (7.21)	0.01
How often use rescue inhaler (M, SD)	2.1 (1.04)	2.3 (1.23)	0.52

Note: M = mean, SD = standard deviation. Sample size of n = 39 for any other inhaler for the item of “how often use rescue inhaler”. Age and “how often use rescue inhaler” were analyzed with analysis of variance. “Inhaler easy to use” and “months on current inhaler” were analyzed with the Mann–Whitney test due to skewness. Sex was analyzed with the Pearson chi-square test. Race/ethnicity and education were analyzed with the Fisher’s exact test.

TABLE 2
Comparisons of outcomes

Variable	Any other inhaler (n = 40)	Trelegy (n = 18)	Univariate P	Multivariate P
TAI (M, SD)	46.8 (3.92)	47.8 (5.91)	0.10	0.34
CAT (M, SD)	15.7 (11.10)	19.8 (7.75)	0.16	0.04
BMQ-necessity (M, SD)	8.4 (3.32)	8.3 (2.67)	0.91	0.97
BMQ-concern (M, SD)	17.0 (5.06)	15.2 (3.44)	0.19	0.24
My medication does not help me very much, (no., %)	5 (12.5)	2 (11.1)	1.00	0.72
I get embarrassed using my medication in public(no., %)	3 (7.5)	1 (5.6)	1.00	0.91
I have unpleasant side effects from my medication (#, %)	1 (2.5)	3 (16.7)	0.08	0.09
My medication interferes with my life a lot (#, %)	1 (2.5)	1 (5.6)	0.53	0.44

Note: M = mean, SD = standard deviation. CAT = COPD Assessment Test, TAI = Test of the Adherence to Inhalers, BMQ = Beliefs about Medicines Questionnaire. Sample size of n = 39 for any other inhaler for CAT. TAI analyzed with the Mann–Whitney test because of skewness. All categorical analyses analyzed by the Fisher’s exact test. Multivariate analyses adjusted for logarithmic transformed months on current inhaler. Continuous outcomes were analyzed with analysis of covariance and categorical outcomes were analyzed with logistic regression.

TABLE 3
Spearman correlation analyses of continuous inhaler variables and outcomes

Variable	1	2	3	4	5	6	7
1–Easy	1.00						
2–Current	-0.01	1.00					
3–Rescue	0.17	0.12	1.00				
4–CAT	0.05	0.29*	0.42**	1.00			
5–TAI	0.02	-0.01	-0.19	-0.10	1.00		
6–BMQ-necessity	-0.11	-0.08	0.04	-0.08	-0.09	1.00	
7–BMQ-concern	-0.06	0.19	-0.31*	0.01	-0.01	0.06	1.00

Note: Easy = inhaler easy to use, current = months on current inhaler, rescue = how often use rescue inhaler, CAT = COPD Assessment Test, TAI = Test of the Adherence to Inhalers, BMQ = Beliefs about Medicines Questionnaire. Sample size of n = 57 for analyses conducted with how often use a rescue inhaler and also CAT.

*P < 0.05.
**P < 0.01.

“medication interferes with my life a lot” did not significantly differ between the Trelegy and the any other inhaler group.

Table 3 shows Spearman correlation analyses. The CAT was positively correlated with months on the current inhaler ($r_s = 0.29, P < 0.05$) and positively correlated with how often use a rescue inhaler ($r_s = 0.42, P < 0.01$). BMQ-concerns were negatively correlated with how often use a rescue inhaler ($r_s = -0.31, P < 0.05$).

DISCUSSION

Our study aim was to determine if there is any difference for Trelegy as compared with multiple inhalers use for adherence, symptoms, medication beliefs, and medication attitudes. We found that patients using Trelegy had greater symptoms compared with the symptoms experienced by the other inhaler group. We did not find a difference between the groups for adherence or any of the medication scales or medication questions. CAT score was positively correlated with the number of months patients were on their current inhaler and their use of a rescue inhaler. Patients with more concerns about their medications were negatively correlated with the use of a rescue inhaler.

We found that those using Trelegy had a CAT score that was significantly higher than those using any other inhaler. Previous research reports that patients who used Trelegy for 6 months had fewer symptoms and improved lung function than those not using Trelegy [24]. Our study differs from these findings as patients reported higher symptoms and used Trelegy for almost 1 year. A possible reason for the difference in findings between our study and the INTREPID trial is that our study had long-term use of more than 6 months and this may result in patient tolerance to Trelegy and, therefore, increased symptoms. It is also possible that the greater symptoms identified in patients using Trelegy during this study are because clinicians may have recommended Trelegy for those with more severe COPD symptoms and whose symptoms were not previously sufficiently controlled by one or more medication inhalers.

DISCLOSURES

Contrary to our hypothesis, we found that those using Trelegy did not differ in their TAI adherence score as compared with those using any other inhaler. Previous research showed that patients taking the COPD medication administered via multiple inhalers were less adherent than patients taking medications administered via a single inhaler [27]. Our study differs from this pattern and may have occurred because of our small sample size as compared to the very large sample size of over 23,000 patients in the aforementioned study. Previous research with a large sample size of over 1,000 patients reports that only approximately 52% of COPD patients show “good” adherence based upon TAI scores, regardless of inhaler type used [20]. In our study with a small sample size both those using Trelegy and those using any other inhaler had high TAI adherence scores. Our study suggests that patients who successfully manage multiple inhalers are adherent to their inhaler regimen and do not need to benefit from a one inhaler approach such as Trelegy.

We found that those using Trelegy did not differ in their medication concerns, medication necessity, and medication attitudes as compared with those using any other inhaler. Previous research with a sample size of over 400 patients reports that BMQ necessity is positively associated with increased adherence for COPD patients [28]. In our study with a small sample size, because both those using Trelegy and those using any other inhaler had high TAI adherence scores that did not differ from each other, it is likely that medication necessity would not differ between those using Trelegy and those using any other inhaler. It is also possible that this reason may apply to medication concerns and medication attitudes.

We found that a higher CAT score indicative of greater symptoms was associated with increased number of months on current inhaler and also more often use of a rescue inhaler. Previous research with a sample size of 2,196 COPD patients reports a positive association between more use of a rescue inhaler and a higher burden of patients’ symptoms as demonstrated by the CAT score [29]. Our findings are similar to this pattern. We suggest that patients are using the rescue inhaler to help relieve some of their symptoms.

We found that more medication concerns specifically related to worries regarding the patients taking their inhalers, the long-term side effects, dependency on their medications, and disruption of life were associated with less use of a rescue inhaler. Previous research among asthma and COPD patients reports that patients who had strong beliefs that medications are harmful were less likely to be adherent to medication treatment recommendations [28]. Our finding for less use of a rescue inhaler is similar to this pattern. We suggest that patients with COPD who have medication concerns are concerned about using their rescue inhaler. Clinicians should consider discussing patients’ medication concerns to address any potential avoidance of rescue inhaler use.

To the best of our knowledge, this is the first study to compare Trelegy with other inhalers for adherence and medication attitudes. This study has some limitations. First, we had a small sample size that may have been underpowered for certain analyses. Second, our survey used self-reported data. Furthermore, we could not observe the inhaler techniques of the patients because we used anonymous surveys. Only self-reported symptoms were recorded and not clinician assessment of COPD severity. Clinician assessment of COPD severity may have impacted inhaler use of patients where those with greater severity may have been prescribed Trelegy.

CONCLUSION

Our study aim was to identify whether there is any difference for Trelegy as compared with multiple inhalers use for adherence, symptoms, medication beliefs, and medication attitudes. We found that patients using Trelegy had greater symptoms in comparison with the any other inhaler group. We did not find any adherence benefit for use of Trelegy. We recommend that clinicians should regularly re-evaluate their Trelegy recommendations, as Trelegy use may not be the best therapy for certain patients. The clinician decision can also consider the cost of Trelegy as compared with other common inhalers. Also, a study with a larger sample size can be beneficial to confirm these findings.

Contributors

HM: study design, data acquisition, data interpretation, drafting manuscript, manuscript approval

JF: study design, data interpretation, data analysis, revising manuscript, manuscript approval

NS: data acquisition, data interpretation, revising manuscript, manuscript approval

RJS: data acquisition, data interpretation, revising manuscript, manuscript approval

JA: study design, data interpretation, revising manuscript, manuscript approval

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Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval

Informed consent was obtained from all participants. The Nassau Health Care Corporation IRB approved the study.

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