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CLINICAL RESEARCH STUDY

Comparing COPD Treatment: Nebulizer, Metered Dose Inhaler, and Concomitant Therapy

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ABSTRACT

PURPOSE: Patients using albuterol and ipratropium for treating chronic obstructive pulmonary disease (COPD) can use either nebulizers or metered dose inhalers. This study compared the 2 methods of delivering medication and the concomitant use of both nebulizer and inhaler, with respect to health-related quality of life, patient symptoms, and efficacy.

SUBJECTS AND METHODS: Patients over 50 years old with COPD were randomized into 3 groups: nebulizer, inhaler, or concomitant treatment. Quality of life was assessed using the St. George's Respiratory Questionnaire at baseline, and at 6 and 12 weeks. Other efficacy measurements at these time-points included pre- and post-dose forced expired volume in 1 second (FEV_1). Symptom scores and peak flow measurements were recorded in patient diaries.

RESULTS: Of 140 patients enrolled, 126 completed at least one post-baseline assessment. At week 6, both groups using a nebulizer achieved statistically significant improvements from baseline in questionnaire symptoms, and the concomitant treatment group had clinically and statistically significant improvement in total questionnaire score. At week 12, the concomitant group still maintained significant improvement in symptom sub-scores. The 3 groups showed little change over time in peak flow or FEV_1, with no significant difference among groups. Both groups using a nebulizer had significant improvement over time in diary symptom scores, although differences between groups were not significant.

CONCLUSIONS: Patients using combined nebulizer therapy morning and night with mid-day inhaler use had the most statistically significant improvements in quality of life indices. This concomitant regimen provides the additional symptom relief offered by a nebulizer with the convenience of an inhaler when patients are away from home.

KEYWORDS: COPD; Metered dose inhaler; Nebulizer; Symptom relief

Chronic obstructive pulmonary disease (COPD) is a disease characterized by airflow obstruction that is not fully reversible, is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily due to cigarette smoking.[1] It can be associated with symptoms of chronic cough, exertional dyspnea, expectoration of sputum, and wheeze. To provide symptomatic management, inhaled bronchodilators are generally recommended.[1,2]

The 2003 Global Initiative for Chronic Obstructive Lung Disease[1] and American Thoracic Society/European Respiratory Society[2] guidelines recommend combination therapy with a β_2-agonist and an anticholinergic for patients not adequately responding to monotherapy. Several studies have demonstrated that this combination of medications is more effective than either agent alone in treating patients with COPD.[3-7] Combinations of albuterol and ipratropium are available either as a metered dose inhaler or a unit dose solution for nebulization.

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These 2 alternative delivery methods have relative advantages and disadvantages, as well as potentially different impacts on treatment outcomes, including health-related quality of life. Nebulizer treatment is often prescribed to patients who prefer nebulizers or demonstrate poor inhaler technique. These patients often are elderly or have problems with coordination. Because nebulizers are not as convenient as inhalers, ambulatory patients may find it more convenient to use inhalers at certain times throughout the day when they are away from home.

Numerous acute bronchospastic studies comparing the efficacy of inhalers versus nebulizers have shown no significant difference.[8,9] However, almost all these studies required precise patient instructions to be followed along with use of spacers or holding chambers with the inhaler. Those clinical trials by their very nature created an artificial environment where patient adherence using spacers was enforced. In a real-life observational study that assessed patients' inhalation techniques using inhalers, frequent improper inhaler use was observed.[10] A comparison of inhalers to nebulizers is needed in the more realistic situation in which patients may or may not have been prescribed spacers and, if prescribed, could choose to use them or not. Studies comparing the impact of these aerosol delivery methods on quality of life are also lacking. The current research was undertaken to investigate differences between methods of delivering maintenance bronchodilator therapy in a naturalistic setting.

CLINICAL SIGNIFICANCE

- Findings suggested that health-related quality of life improved when COPD patients used a combination of a nebulizer morning and night, and a metered dose inhaler in the afternoon and evening.
- This combination provides the benefits of additional symptom relief offered by the nebulizer, as well as the convenience of the metered dose inhaler when patients are away from home.

STUDY OBJECTIVES

The purpose of this study was to compare the impact on quality of life, patient symptoms, and other outcomes of maintenance treatment of COPD using a nebulizer versus an inhaler only or the concomitant use of a nebulizer and inhaler versus an inhaler only to deliver the same medication. The medication used was a combination of albuterol and ipratropium in the form of DuoNeb (Dey; Napa, California) for the nebulizer and Combivent (Boehringer Ingelheim Pharmaceuticals; Ridgefield, Connecticut) for the inhaler.

METHODS AND MATERIALS

Study Design

Patients were recruited into a 12-week, multi-center, single-blind, 3-arm, parallel-group, phase 4 study conducted in 2004. Study-eligible patients were randomized into one of 3 treatment groups, each allowing albuterol inhaler rescue medication as needed:

- Nebulizer (albuterol plus ipratropium unit dose solution; DuoNeb) only, 1 unit dose vial 4 times daily
- Inhaler (albuterol plus ipratropium; Combivent) only, 2 puffs 4 times daily
- Concomitant treatment involving nebulizer (morning and night) plus inhaler (afternoon and evening)

Inclusion and Exclusion Criteria. Eligible patients included men and women over 50 years of age who met the American Thoracic Society/European Respiratory Society definition of COPD,[2] had a history of >10 pack-years of cigarette smoking, and had a best post-bronchodilator forced expiratory volume in 1 second (FEV_1) >30% and <65% of predicted[11,12] and a post-bronchodilator FEV_1/forced vital capacity ratio <70%. Exclusion criteria included the diagnosis of asthma, parenchymal lung disease apart from COPD, polycythemia, cor pulmonale, significant hypoxemia requiring domiciliary oxygen therapy, history of a thoracotomy, hospitalization within the past 2 months for COPD, clinically significant obstructive urinary disease, narrow-angle glaucoma, unstable angina, myocardial infarction in the past 6 months, or other serious medical illness that would interfere with the patients' participation in the trial. Excluded medication included concomitant long-acting β-agonists, long-acting anticholinergics, nonselective β-blockers, or additional ipratropium via inhaler or nebulizer.

Study Variables. The primary outcome variable was quality of life measured by the validated, self-administered St. George's Respiratory Questionnaire,[12] completed at baseline, 6 weeks, and 12 weeks. Three component sub-scores were calculated: *Symptoms* (ie, respiratory symptoms and their frequency and severity), *Impacts* (ie, social functioning and psychological disturbances resulting from COPD), and *Activity* (ie, activities causing, or limited by, breathlessness). A Total score from 0 to 100 summarized the impact of the disease on overall health status, 0 and 100 representing the best and worst possible health, respectively. The threshold for a clinically significant difference in Total score (and also for the Impacts sub-score) between groups of patients, and for changes within groups, is 4 units.[12]

Additional study endpoints included Patient Symptom Score and other efficacy measurements (home morning and nighttime daily peak flow before dosing with study medication and pre- and post-dose FEV_1 in the clinic). Daily peak flow measurements and patient symptoms were obtained during a 2-week run-in period and throughout the

12-week treatment period. Clinic spirometry before and after dosing with study medication was performed at baseline and the 6- and 12-week follow-up visits. Throughout the trial, patients were repeatedly instructed in correct techniques for inhaler and nebulizer use.

The Patient Symptom Score was derived from a patient diary in which patients self-scored 6 symptoms (ability to perform daily activities; breathlessness over the past 24 hours; waking at night due to respiratory symptoms; breathlessness on arising; cough; and sputum production).[13] Each symptom was scored daily on a 4-point scale (0 = best to 3 = worst); scores were summed to obtain the total daily score from 0 to 18. Total scores were averaged over the 12-week treatment period.

Safety measures included vital signs, changes in physical findings, investigator-reported disease exacerbation, and adverse events.

Analysis Methods

All randomized patients receiving at least one dose of study medication were included in the intent-to-treat population. Randomized patients who received at least one dose and completed at least one questionnaire post-baseline (ie at week 6 or 12) were included in the analysis.

Fisher's exact test was used for pair-wise comparisons of age, sex, and race across treatment groups. Total scores and sub-scores from the health status questionnaire and total symptoms scores from the daily diaries were compared using 2-sided *t*-tests at each time point.

For tests involving pre- and post-dose FEV_1 measurements, which had skewed distributions, log transformations were first used on each variable to create more normally distributed sets of values before differences were calculated between treatment groups.

Last nonmissing observations were carried forward for missing week 12 values for patients with observations at both baseline and week 6.

RESULTS

Patient Sample and Demographics

A total of 140 patients were enrolled across 17 sites, with 126 patients (90%) completing at least one post-baseline assessment (the analytic population) and 97 (69%) finishing the entire study. The most common reason for early discontinuation was withdrawal of consent (56%). The analytic population was divided nearly evenly among the 3 treatment groups, with demographic characteristics similar in all 3 groups (Table 1).

Health-Related Quality of Life

Table 2 shows that quality of life, as measured by the questionnaire Total score at baseline, was similar in all 3 groups, as were the Symptoms, Impacts, and Activity subscores. The only difference that approached statistical significance was between the concomitant treatment group and the inhaler-only group for Symptoms ($P = .056$).

After 6 weeks of treatment, the change from baseline in Total Quality of Life score (Table 3) exceeded the 4-unit threshold for clinically significant improvement in the concomitant treatment group, and the nebulizer-only group approached this level of clinical improvement. Differences *between* the treatment groups in the amount of change were not statistically significant. Differences *within* treatment groups from baseline to week 6 were statistically significant ($P = .0196$) only for the concomitant treatment group.

Statistically significant improvement was also seen in Symptoms sub-scores at week 6 for patients using a nebulizer only or concomitant treatment ($P = .019$ and $P < .004$, respectively) (Table 3). Change from baseline (mean ± SE) for the inhaler-only group (-3.0 ± 3.04) did not reach statistical significance. Only the concomitant therapy group achieved clinically significant improvement in Impacts subscore at week 6 (-5.1 ± 3.00), but this change from baseline to week 6 was not statistically significant (Table 3). The inhaler-only group did show statistically significant improvement in the Impacts sub-score ($P = .0283$), but this

Table 1 Baseline Characteristics

Baseline Characteristic		Nebulizer (n = 37)	Nebulizer and Inhaler (Concomitant Treatment) (n = 46)	Inhaler (n = 43)	Total Analytic Population (n = 126)	*P* Value Comparing*	
						Nebulizer vs Inhaler	Concomitant Treatment vs Inhaler
Age (years)	Mean	65.9	62.5	62.3		.0565	.7895
	(SE)	(1.38)	(1.51)	(1.34)			
Sex, n (%)	Male	19 (51)	27 (59)	23 (53)	69 (55)	1.000	.672
	Female	18 (49)	19 (41)	20 (47)	57 (45)		
Race, n (%)	Caucasian	33 (89)	43 (93)	34 (79)	110 (87)	.230	.078
	African American	3 (8)	3 (7)	8 (19)	14 (11)		
	Hispanic	1 (3)	0	0	1 (1)		
	Asian	0	0	0	0		
	Other	0	0	1 (2)	1 (1)		

SE = standard error of the mean.
**P* values are based on a Fisher's exact test comparing either nebulizer vs inhaler or concomitant treatment vs inhaler.

Table 2 Health-Related Quality of Life Measured by St. George's Respiratory Questionnaire at Baseline

Score		Nebulizer (n = 37)	Nebulizer and Inhaler (Concomitant Treatment) (n = 46)	Inhaler (n = 43)	*P* Value Comparing* Nebulizer vs Inhaler	*P* Value Comparing* Concomitant Treatment vs Inhaler
SGRQ Total	n	34	44	40	.874	.612
	Mean (SE)	47.7 (2.96)	50.2 (2.57)	48.3 (2.70)		
SGRQ Symptoms	n	37	46	43	.798	.056
	Mean (SE)	63.4 (3.35)	70.1 (2.48)	62.2 (3.27)		
SGRQ Impacts	n	34	44	40	.537	.955
	Mean (SE)	35.0 (3.45)	38.1 (3.22)	37.9 (3.13)		
SGRQ Activity	n	36	45	40	.530	.533
	Mean (SE)	60.8 (3.41)	60.5 (2.73)	58.0 (2.89)		

SGRQ = St. George's Respiratory Questionnaire; SE = standard error of the mean.
**P* values are based on a 2-sided *t* test for difference in means comparing either nebulizer vs inhaler or concomitant treatment vs inhaler.

was not clinically significant (-3.3 ± 2.26). There were no significant differences between the treatment groups in the changes between baseline and week 6 in Total score or any of the sub-scores.

At week 12, only the concomitant therapy group approached clinically significant improvement in Total score (-3.5 ± 2.64) (Table 4). Both the concomitant treatment group and the nebulizer-only group showed sizeable improvement in the Symptoms sub-score, and the changes in this sub-score from baseline in the concomitant group were statistically significant ($P = .0186$). The inhaler-only group had a much smaller change in the Symptoms sub-score, and in the opposite direction. None of the treatment groups reached clinically significant improvement in the Impacts sub-score. The only difference within treatment groups at week 12 that was statistically significant was the improvement in the Symptoms sub-score for the concomitant group. Compared with the change in Symptoms sub-score for the inhaler group, the change in this sub-score for the concomitant treatment group was of borderline significance ($P = .0637$). No other changes from baseline to week 12 differed significantly between treatment groups.

Peak Flow

There were no appreciable changes from baseline or pairwise differences between treatment arms at weeks 6 or 12 in peak flow measurements.

Pre-and Post-Bronchodilator FEV_1

Tables 5 and 6 show pre- and post-bronchodilator FEV1 values at baseline, week 6, and week 12. At baseline, differences between the groups were not statistically significant. Changes pre- and post-bronchodilator FEV_1 within the treatment groups were not statistically significant at either 6 or 12 weeks; only the inhaler-only group showed a statis-

Table 3 Change in Health-related Quality of Life Measured by St. George's Respiratory Questionnaire at Week 6

Score		Nebulizer (n = 37)	Nebulizer and Inhaler (Concomitant Treatment) (n = 46)	Inhaler (n = 43)	*P* Value Comparing* Nebulizer vs Inhaler	*P* Value Comparing* Concomitant Treatment vs Inhaler
SGRQ Total	n	21	31	35		
	Mean (SE)	−3.7 (2.21)†	−5.2 (2.33)	−2.1 (1.78)†		
			P = .0196†		.5835	.2873
SGRQ Symptoms	n	27	35	39		
	Mean (SE)	−9.2 (3.58)	−9.3 (3.06)	−3.0 (3.04)†		
		P = .0190†	*P* = .0039†		.1927	.1502
SGRQ Impacts	n	21	32	35		
	Mean (SE)	−1.1 (3.06)†	−5.1 (3.00)†	−3.3 (2.26)		
				P = .0283†	.5572	.6264
SGRQ Activity	n	25	34	36		
	Mean (SE)	−0.7 (3.03)†	−3.5 (2.21)†	2.3 (2.29)†	.4200	.0733

SGRQ = St. George's Respiratory Questionnaire; SE = standard error of the mean.
**P* values are based on a 2-sided *t* test for difference in means comparing either nebulizer vs inhaler or concomitant treatment vs inhaler.
†*P* values, based on a 2-sided paired *t* test to compare log-transformed means of observations within treatment groups for baseline and week 6, are not significant unless shown.

Table 4 Change in Health-related Quality of Life Measured by St. George's Respiratory Questionnaire at Week 12

Score		Nebulizer (n = 37)	Nebulizer and Inhaler (Concomitant Treatment) (n = 46)	Inhaler (n = 43)	*P* Value Comparing* Nebulizer vs Inhaler	*P* Value Comparing* Concomitant Treatment vs Inhaler
SGRQ Total	n	29	40	36		
	Mean (SE)	−1.6 (2.14)†	−3.5 (2.64)†	−2.4 (1.92)†	.7758	.7488
SGRQ Symptoms	n	32	43	40		
	Mean (SE)	−4.0 (3.83)†	−6.1 (3.00) *P* = .0186†	2.0 (3.13)†	.2209	.0637
SGRQ Impacts	n	29	42	36		
	Mean (SE)	0.7 (2.52)†	−3.2 (3.37)†	−3.7 (2.34)†	.2087	.9109
SGRQ Activity	n	31	42	37		
	Mean (SE)	−3.1 (2.51)†	−2.9 (2.00)†	−0.5 (2.32)†	.4359	.4256

SGRQ = St. George's Respiratory Questionnaire; SE = standard error of the mean.

**P* values are based on a 2-sided *t* test for difference in means comparing either nebulizer vs inhaler or concomitant treatment vs inhaler.

†*P* values, based on a 2-sided paired *t* test to compare log-transformed means of observations within treatment groups for baseline and week 12, are not significant unless shown.

tically significant change from baseline at week 6 ($P = .0060$) (Table 5).

Patient Symptom Scores

Mean Patient Symptom Scores (Table 7) were similar among the treatment groups at baseline. All 3 groups demonstrated improvement in mean Patient Symptom Scores from baseline to week 6 and week 12, with the greatest change seen in the concomitant treatment group at both time points. The change for the concomitant group was significant at both time points ($P < .05$), and the change was also significant for the nebulizer-only group at week 12 ($P < .05$) and of borderline significance at week 6 ($P = .0539$). No significant between-group differences in the changes in Patient Symptom Scores were noted.

DISCUSSION

While randomized controlled trials have failed to show significant differences between nebulizers and inhalers for delivering bronchodilator therapy in their effects on lung function or respiratory symptoms,[9] these trials had a number of limitations. Shortcomings included study populations restricted to those demonstrating ability to use the devices properly, failure to take patient preferences into account, and limited study of how long-term real-life use affected clinically important outcomes other than lung function, such as health-related quality of life, patient satisfaction, and device preferences. A recent study surveying patients' views of home nebulizer therapy for chronic lung diseases found that patients receiving such therapy reported overwhelmingly (98% vs 2%) that perceived benefits from using a nebulizer over an inhaler (eg, improved breathing, greater self-confidence, less need to contact health care providers) outweighed perceived disadvantages (eg, longer time required for nebulizer treatment and cleaning the device).[10]

The current study compared the effects of nebulizer versus inhaler use, and their concomitant use, on quality of life and more commonly assessed efficacy endpoints. All 3

Table 5 Pre-Bronchodilator FEV_1 at Baseline, Week 6, and Week 12

Pre-FEV_1		Nebulizer (n = 37)	Nebulizer and Inhaler (Concomitant Treatment) (n = 46)	Inhaler (n = 43)	*P* Value Comparing Nebulizer vs Inhaler	*P* Value Comparing Concomitant Treatment vs Inhaler
Baseline, L	n	31	40	40		
	Mean (SE)	1.1 (0.09)	1.2 (0.09)	1.3 (0.09)	.1344*	.8524*
Week 6, L	n	27	35	37		
	Mean (SE)	1.2 (0.12)†	1.3 (0.10)†	1.4 (0.10) *P* = .0060†	.1444*	.4085*
Week 12, L	n	27	35	33		
	Mean (SE)	1.2 (0.10)†	1.2 (0.09)†	1.2 (0.09)†	.5846*	.8114*

SE = standard error of the mean.

**P* values are based on a 2-sided *t* test for difference in means comparing either nebulizer vs inhaler or comcomitant treatment vs inhaler.

†*P* values, based on a 2-sided paired *t* test to compare log-transformed means of observations within treatment groups for baseline and week 6 and baseline and week 12, are not significant unless shown.

Table 6 Post-Bronchodilator FEV_1 at Baseline, Week 6, and Week 12

Post-FEV_1		Nebulizer (n = 37)	Nebulizer and Inhaler (Concomitant Treatment) (n = 46)	Inhaler (n = 43)	*P* Value Comparing: Nebulizer vs Inhaler	*P* Value Comparing: Concomitant Treatment vs Inhaler
Baseline, L	n	31	40	40		
	Mean (SE)	1.2 (0.08)	1.4 (0.09)	1.4 (0.09)	.0774*	.9088*
Week 6, L	n	26	36	37		
	Mean (SE)	1.3 (0.13)†	1.4 (0.11)†	1.5 (0.11)†	.2631*	.6115*
Week 12, L	n	26	35	33		
	Mean (SE)	1.2 (0.10)†	1.3 (0.09)†	1.3 (0.09)†	.1634*	.9434*

SE = standard error of the mean.

**P* values are based on a 2-sided *t* test for difference in means comparing either nebulizer vs inhaler or concomitant treatment vs inhaler.

†*P* not significant based on a 2-sided paired *t* test to compare log-transformed means of observations within treatment groups for baseline and week 6 and baseline and week 12.

treatment groups had similar demographic characteristics, quality of life, diary symptoms, and FEV_1 at baseline. The most apparent differences across the study treatment regimens were noted at 6 weeks, when both groups using a nebulizer achieved statistically significant improvements from baseline in the quality-of- life Symptoms sub-score, and the group receiving concomitant treatment showed both clinically and statistically significant improvement in quality-of-life Total score. Also at week 6, the nebulizer-only group approached clinically significant improvement in Total score, but the group using an inhaler alone showed no clinically significant improvements in this score. Improvements in the groups using a nebulizer were no longer as consistent at week 12, when the only statistically significant improvement from baseline was for the quality-of-life Symptoms sub-score in the concomitant treatment group.

Although apparent differences in quality of life were observed between the nebulizer groups and the inhaler-only group, the 3 groups were remarkably similar for changes in peak flow, pre- and post-bronchodilator FEV_1, and diary symptom scores.

Thus, while providing similar clinical efficacy regarding lung function and diary-recorded symptoms, use of the nebulizer, both alone and in combination with an inhaler, appeared to offer benefits over the inhaler alone in quality of life, as reflected by clinically meaningful and statistically significant reductions in symptoms scores by concomitant therapy patients at 6 and 12 weeks. This apparent disparity between better symptom control and no difference in bronchodilator efficacy, as measured by spirometry and peak flow measurements, has been noted previously in patients with COPD. For example, Mahler et al[14] showed poor correlation between FEV_1 and symptoms of breathlessness measured by the Baseline Dyspnea Index. A possible explanation for the disparity between changes in symptoms and FEV_1 may be that the longer duration of inhaling larger doses of bronchodilators by nebulization compared with inhaler could lead to more effective reduction in resting and dynamic hyperinflation despite similar changes in FEV_1, thus improving exercise tolerance and perceived breathlessness during exertion.[15]

Table 7 Total Patient Symptom Scores at Baseline, Week 6, and Week 12

Score		Nebulizer (n = 37)	Nebulizer and Inhaler (Concomitant Treatment) (n = 46)	Inhaler (n = 43)	*P* Value Comparing: Nebulizer vs Inhaler	*P* Value Comparing: Concomitant Treatment vs Inhaler
Baseline	n	35	45	43		
	Mean (SE)	5.8 (0.60)	5.6 (0.52)	5.8 (0.53)	.9914*	.7502*
Week 6	n	30	38	39		
	Mean (SE)	4.6 (0.57)	3.9 (0.51)	4.5 (0.50)†	.9472*	.3852*
		P = .0539†	*P* = .0312†			
Week 12	n	30	37	39		
	Mean (SE)	4.8 (0.64)	4.3 (0.57)	4.8 (0.56)†	.9882*	.5016*
		P = .0461†	*P* = .0490†			

SE = standard error of the mean.

**P* values are based on a 2-sided *t* test for difference in means comparing either nebulizer vs inhaler or concomitant treatment vs inhaler.

†*P* values, based on a 2-sided paired *t* test to compare log-transformed means of observations within treatment groups for baseline and week 6 and baseline and week 12, are not significant unless shown.

The trend observed in the present study toward better symptom improvement with nebulizers compared with inhalers is consistent with previously reported findings. For example, in a survey of patients on nebulizer therapy, patients reported that the benefits of using nebulizers, particularly symptom control, outweighed the disadvantages, which included restrictions due to their limited portability.[16] Moreover, in a crossover study in which elderly patients with chronic airflow obstruction received bronchodilator therapy for 2 weeks by either nebulizer or inhaler in random order, patients clearly indicated preference for the nebulizer with respect to subjectively perceived effectiveness (despite the absence of any objective spirometric evidence of differences in bronchodilator efficacy), although they rated the inhaler as more convenient.[9]

Study Limitations

The present study has some limitations. Because the study could not be double-blinded, we cannot control for possible subjects' bias toward nebulizer therapy. Because the major endpoints of the study were subjective (self-reported quality of life and symptom scores), these outcomes could have been affected by potential patients' bias that nebulizer therapy is more effective than an inhaler alone. Another limitation of the study is that, currently, only short-acting adrenergic and anticholinergic solution bronchodilators are available for nebulizer use, and the impact on quality of life and symptoms of these solution bronchodilators in combination were compared with the same short-acting bronchodilators delivered in combination from a single metered-dose inhaler. However, long-acting inhaled bronchodilators, both twice-daily long-acting beta-agonists (salmeterol and formoterol) and a once-daily long-acting anticholinergic bronchodilator (tiotropium) are currently available in separate dry-powder devices, although not in combination. Further studies would be required to compare the impact on patient-centered outcomes of these long-acting agents administered separately twice or once daily with nebulized short-acting bronchodilators administered in combination 4 times daily or twice daily (morning and nighttime) in conjunction with a short-acting combination inhaler twice daily (afternoon and evening). In the future, long-acting solution bronchodilators may also become available for nebulizer use.

CONCLUSIONS

In this naturalistic study, the most effective regimen for managing COPD and improving patient quality of life appeared to be the combined use of a nebulizer in the morning and at night, and an inhaler in the afternoon and evening. Although patients may consider use of an inhaler alone to be more convenient than using only a nebulizer, the combination of treatment modalities offers potential advantages. Such a regimen could provide the benefits of additional symptom relief offered by the nebulizer, as well as the greater convenience of allowing the inhaler to be used when patients are away from home during the day.

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