The effect of twice daily aclidinium bromide/formoterol fumarate 340/12 mcg vs. once daily tiotropium 'respimat' 5mcg on static and dynamic hyperinflation in patients with COPD during 24 hours.

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Therefore we aimed to study the 24 hour effect of twice daily aclidinium/formeterol versus once daily tiotropium on serial static and dynamic lung hyperinflation measurements, as well as (24 hour) symptoms and sleep quality. Tiotropium was chosen as...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON49226

Source
ToetsingOnline

Brief title
BOTH study (BrOchodilaTion Hyperinflation)

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Chronic obstructive pulmonary disease (COPD)

Research involving
Human

Sponsors and support

Primary sponsor: CIRO+, expertisecentrum voor chronisch orgaanfalen
Source(s) of monetary or material Support: AstraZeneca

Intervention

Keyword: Bronchodilation, Hyperinflation, Physical activity, Sleep quality

Outcome measures

Primary outcome

To explore the effect of of aclidinium/formoterol 340/12 mcg DPI twice daily compared to tiotropium respimat 5 mcg PMDI once daily on 24 hour static hyperinflation.

Secondary outcome

To explore the effect of of aclidinium/formoterol 340/12 mcg DPI twice daily compared to tiotropium respimat 5 mcg PMDI once daily on 24 hour spirometry.
To explore the effect of of aclidinium/formoterol 340/12 mcg DPI twice daily compared to tiotropium respimat 5 mcg PMDI once daily on 24 hour dynamic hyperinflation.
To explore the effect of aclidinium bromide/formoterol fumarate 340/12 mcg DPI twice daily compared to tiotropium respimat 5mcg PMDI once daily on 24 hour respiratory symptoms.
To explore the effect of aclidinium bromide/formoterol fumarate 340/12 mcg DPI twice daily compared to tiotropium respimat 5mcg PMDI once daily on sleep quality.
To explore the effect of aclidinium bromide/formoterol fumarate 340/12 mcg DPI twice daily compared to tiotropium respimat 5mcg PMDI once daily on nighttime

physical activity, as an inverse surrogate for sleep quality.

Study description

Background summary

Exertional dyspnea is the most important symptom of COPD patients. Exertional dyspnea is multifactorial, but derangement of ventilator mechanics due to lung hyperinflation (LH) is thought to play an important role. Static LH causes an upward shift in the pressure-volume curve, where there is increased elastic loading, due to loss of elastic properties of the lung without loss of the elastic properties of the chest wall. Together with increasing intrathoracic gas volume, the residual volume also increases, due to premature closure of the small airways, a feature otherwise known as gas or air trapping. Static LH is highly predictive for dynamic LH, a situation where the end-expiratory lung volume increases during exercise due to reduced lung elastance and insufficient time to deflate the lungs. Dynamic LH is importantly related to exertional dyspnea and exercise limitation and is the major contributing factor of physical inactivity in COPD, regardless of their BODE or GOLD classification. Bronchodilation therapy is the cornerstone of the treatment of patients with COPD as it reduces dyspnea, increases exercise capacity, and improves quality of life in individuals with COPD. Randomized controlled trials have been evaluated consistently by spirometric outcomes, mostly forced expiratory volume in the first second. Also, the pharmacological effects of different products on lung hyperinflation outcomes were increasingly studied in recent years. However, there is no information on the 24 hour effect of pharmacotherapy on static lung hyperinflation and a twice daily compared to once daily regimen has not been studied. In addition dual to single bronchodilator therapy has only been scarcely studied and results were contradictory.
It has been established that COPD symptoms vary throughout the day, but there is a scarcity of information of long-acting bronchodilation on 24 hour symptoms in COPD patients. Also, sleep quality is known to be poor in COPD patients, with increased nocturnal symptoms. Recently, it was shown that tiotropium is associated with decreased COPD-related night-time awakenings. Night-time awakenings were associated with increased nocturnal rescue medication use. Also, a significant improvement of overall night-time and early-morning symptom severety and limitation of early-morning activities were observed with aclidinium bromide/formoterol fumarate 340/12 µg and both monotherapies.

Study objective

Therefore we aimed to study the 24 hour effect of twice daily aclidinium/formeterol versus once daily tiotropium on serial static and dynamic lung hyperinflation measurements, as well as (24 hour) symptoms and sleep

quality.
Tiotropium was chosen as a comparator because it has developed as the gold standard for long acting bronchodilator therapy for research.

Study design

Experimental, randomized, 2-arm, cross-over study.

Intervention

Aclidinium bromide/formoterol fumarate (Duaklir Genuair), 1 dose of 340/12mcg per 12 hours via DPI. Tiotropium (Spiriva Respimat), 2 doses of 2,5 mcg once per 24 hours via PMDI.

Study burden and risks

This exploratory study will be performed using two kinds of medications which are already registered for treatment of COPD. Therefore, the risks are minimal and predictive.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients with COPD with static hyperinflation above the higher limit of normal defined as 1,64 times the standard deviation above the predicted value.

Exclusion criteria

Patients treated with oral corticosteroids and/or antibiotics for an exacerbation and/or lower respiratory tract infection in the 4 weeks prior to screening.
Patients with hypercapnia (>= 6.5 kPa).
Patients unable to perform bodybox measurements
Known respiratory disorders other than COPD which may impact the efficacy of the study drug.
Patients with clinically significant cardiovascular conditions.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-06-2017
Enrollment:	49
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Duaklir Genuair
Generic name:	Aclidinium bromide/Formoterol fumarate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Spiriva Respimat
Generic name:	Tiotropium Respimat
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-05-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-02-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-06-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-06-2019
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-01-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-003989-12-NL
CCMO	NL59452.100.16