Morphine or Fentanyl for Refractory dyspnea in COPD

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

Summary

ID

NL-OMON52406

Source
ToetsingOnline

Brief title
MoreFoRCOPD

Condition

- Bronchial disorders (excl neoplasms)

Synonym
chronic bronchitis and emphysema., COPD (Chronic Obstructive Pulmonary Disease)

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Innovatiefonds zorgverzekeraars en Stichting Astma Bestrijding

Intervention

Keyword: COPD, Dyspnea, Fentanyl, Morphine

Outcome measures

Primary outcome

The primary endpoint is change in average dyspnea sensation as measured on the Numeric Rating Scale for Dyspnea, mean of daily measurements for days 7 to 14 of each treatment period.

Secondary outcome

Secondary endpoints are:

Change in worst dyspnea sensation as measured on the Numeric Rating Scale for Dyspnea8, mean of daily measurements for days 7 to 14 of each treatment period.

Change in Health-Related Quality of life (CCQ-questionnaire, mean of daily measurements for days 7 to 14 of each treatment period; CRQ-questionnaire total score; CRQ-questionnaire, domain Mastery)

Anxiety (HADS-A questionnaire)

Side effects (Reported spontaneously in a daily patient diary and asked specifically, both open and named side effects at planned visits. Specifically named side effects are obstipation, nausea, vomiting, drowsiness and dizziness)

Change in hypercapnia, HCO3 en pH (Capillary blood gas analysis)

Change in Sleep quality (Change on a Numeric Rating Scale, mean of daily measurements for days 7 to 14 of each treatment period.)

Patient preference (Which of the three treatment periods the patient preferred. Asked at the end of the third treatment period)

Continued opioid use (Asked three months after the end of the treatment

period)

Study description

Background summary

The most important complaint in severe COPD is dyspnea which is associated with a diminished exercise tolerance and can give anxiety and depression. If the dyspnea continues to exist despite optimal therapy it is called refractory dyspnea. There is evidence that morphine is effective and can safely be prescribed for treating refractory dyspnea. However, a Dutch study recently showed that few pulmonologists actually prescribe opioids for this indication. The main reasons for this are concerns about side effects and respiratory insufficiency as well as negative emotions for the patient and families at the thought of using morphine. We think it*s important to investigate opioids for patients with severe COPD who suffer from refractory dyspnea to improve palliative care in this patient category.
Most studies with opioids for treatment of dyspnea are conducted with morphine tablets, and only a part of these patients suffered from COPD. To our knowledge there has not been a randomized controlled trial investigating fentanyl patches for refractory dyspnea in COPD patients. However, studies comparing fentanyl and morphine in pain management show that patients may prefer fentanyl patches and have less problems with obstipation.

Study objective

There are two main objectives for this study.
First, we will investigate the following hypothesis: Fentanyl patches provide reduction of dyspnea compared to placebo, comparable to morphine, and with less side effects than morphine.
Secondly, with this Dutch multi-center study we would like to enlarge the evidence base and contribute to the experience with opioids for refractory dyspnea in COPD thereby greatly facilitating its implementation in the Netherlands.
Thirdly, we will develop and evaluate educational material about opioid use for dyspnea in COPD to greatly enhance the implementation of opioids for this indication.

Study design

This is a multi-center double blind, double-dummy cross-over randomized placebo-controlled trial with three study arms. A total of 60 COPD patients will be included in this study.

Intervention

Patients will be treated sequentially with three combinations of medication and/or placebo medication in a random order. Each combination will be prescribed for eleven days, with an three interval inbetween as an wash out period.
They will receive either a Fentanyl patch in combination with placebo tablets, a placebo patch with Morphine Slow release tablets or a placebo patch with placebo tablets. Fentanyl will be prescribed in a dosage of 12 µg/hr, the patch will be replaced every three days. The morphine Slow Release will be prescribed in a dosage of 10 mg twice daily.

Study burden and risks

Patients will receive all necessary care and treatments as per normal routine. There will be five visits to the hospital, of which the first probably during routine consultation. Participants will undergo a spirometry and arterial blood gas analysis once. A capillary blood gas will be performed four times. They will be asked to fill out three questionnaires four times. Additionally, patients will receive a diary in which they will be asked to fill out a questionnaire and Numeric Rating Scale for dyspnea, sleep quality and obstipation daily. Both Fentanyl patches and Morphine Slow Release tablets are well known and widely prescribed opioids for different indications. Common side effects include obstipation, nausea and drowsiness. As per routine care when prescribing opioids, patients will receive a laxative, and an antiemetic which they can use as needed. Hypoventilation is an unwanted side-effect that can occur with opioids, but its likelihood is probably overrated by physicians at current doses (Ekström BMJ 2014). To document any occurrence, capillary blood gas analyses will be performed during the study.

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

• Age >=40 years
• Read, understood and signed the Informed Consent form
• COPD GOLD class III or IV, according to GOLD criteria.
- Post-bronchodilatation FEV1/FVC < 70% and FEV1 < 50% pred.
• Complaints of refractory dyspnea as established by patient and doctor.
• mMRC score >= 3.
• Life expectancy of >= 2 months.
• Optimized standard therapy according to Dutch LAN guideline for diagnosis and treatment of COPD.

Exclusion criteria

• Other severe disease with chronic pain or chronic dyspnea (a non-susbstantial component of left sided heart failure is acceptable).
• Current use of opioids for whatever indication
• Allergy / intolerance for opioids
• Psychiatric disease, not related to severe COPD.
• Exacerbation of COPD eight weeks prior to inclusion or between screening and randomization.
• Problematic (leading to medical help or social problems) substance abuse during the last five years.
• Active malignancy, with the exception of planocellular or basal cell carcinoma of the skin.
• eGFR 15 ml/min

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	18-11-2019
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Fentanyl Sandoz Matrix
Generic name:	Fentanyl
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Morphine HCl retard 10 mg
Generic name:	Morphine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	19-11-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	17-04-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-03-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-06-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-01-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-01-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
Other	Aanvraag staat in, nummer volgt

Register	ID
EudraCT	EUCTR2018-002466-39-NL
CCMO	NL66343.042.18