A randomized, placebo and active comparator (oxycodone)-controlled study on the effect of tapentadol on respiration and analgesia in healthy volunteers

Published: 20-03-2014
Last updated: 20-04-2024

The objective of this study is to investigate the extent of respiratory depression at equi-analgesic dosages of tapentadol and oxycodone

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON44407

Source
ToetsingOnline

Brief title
The Restiration study

Condition

- Other condition

Synonym
Respiratory depression and reduced breathing

Health condition

Opioid geïnduceerde ademdepressie

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Grünenthal

Intervention

Keyword: Analgesia, Oxycodone, Respiration, Tapentadol

Outcome measures

Primary outcome

Degree of respiratory depression defined as a decrease in the slope of the Ventilation-CO2 curve, a rightward shift of the Ventilation-CO2 curve and extrapolations at fixed et-CO2 (7 and 9 kPa), resting ventilation and resting end-tidal PCO2.

Secondary outcome

A comparison of the degree of anti-nociception defined as the change in pain pressure threshold.

Study description

Background summary

This novel potent opioid tapentadol (PallexiaTM) has a combined mechanism of action where the single molecule acts at the *-opioid receptor (MOR) at spinal and supraspinal sites and inhibits the reuptake of noradrenaline (NRI) in the spinal cord. The combination of these two mechanisms has been designated as the MOR-NRI concept. The affinity of tapentadol for the *-opioid receptor is 50-fold lower than that of morphine. However, due to synergy between the two mechanisms of action, tapentadol produces potent analgesia by reducing ascending nociceptive trafficking to the thalamus and is useful in the treatment of moderate to severe acute and chronic pain. Tapentadol*s very low affinity for the *-opioid receptor is an advantage as it coincides with a limited side effect profile. Whether this also holds true for the respiratory effects of tapentadol has not been studied yet. A potent analgesic with opioidergic mechanisms with a limited respiratory depressant effect is of large

value as current opioid analgesics without any exception produce potent and long-term respiratory depressant effects. Opioids are considered by the FDA and the APSF (American Patient Safety Foundation) dangerous in the sense that potential life threatening respiratory depression is an inherent property of these drugs.

Study objective

The objective of this study is to investigate the extent of respiratory depression at equi-analgesic dosages of tapentadol and oxycodone

Study design

A randomized, placebo and active comparator controlled study

Intervention

Oral administration of tablet: tapentadol (100 en 150 mg), oxycodone (20mg) and placebo

Study burden and risks

The research is conducted in the anesthesiology department of a university hospital, where all the necessary procedures are followed. The study will be conducted by researchers with experience in the treatment of respiratory depression. Naloxone injections are available in case of severe respiratory depression and other measures to support the respiratory and hemodynamics are available, such as administering fluids, oxygen and vasopressors. Cardiovascular emergency measures such as defibrillation, magnesium sulfate (IV) and antiarythmics are available. The overall risk / benefit analysis is considered acceptable under the circumstances described above

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

Healthy male and female subjects;Age of 18 to 45 years (inclusive);;Body Mass Index (BMI) between 18 and 35 kg/m2 (inclusive) and body weight between 50 kg and 100 kg (inclusive);
Subject is able to read and understand the written consent form, complete study-related procedures, and communicate with the study staff;
Subject is willing to comply with study restrictions.

Exclusion criteria

Clinically relevant abnormal history of physical and mental health, as determined by medical history taking and physical examinations obtained during the screening visit and/or prior to the administration of the initial dose of the study drug (as judged by the investigator);;A semi recumbent systolic blood pressure of >160 mmHg and/or diastolic blood pressure of > 95 mmHg at screening;;History of alcoholism or substance abuse within three years prior to screening;;Positive pregnancy test;;Positive drug screening or alcohol breath test;;Subjects using more than 21 units of alcohol per week;;Use of medication during the study period;;If sexually active, the subject is not using contraceptives, or surgically sterilized;;Subject has a history of severe allergies, or has had an anaphylactic reaction or significant intolerability to prescription or non-prescription drugs or food;;Participation in an investigational drug trial in the 2 months prior to administration of the initial dose of study drug or more than 5 times per year;;Any other condition that in the opinion of the investigator would complicate or compromise the study, or the well being of the subject:

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-11-2015
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Oxycodone
Generic name:	Oxycodon
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Pallexia
Generic name:	tapentadol

Ethics review

Approved WMO

Date:	20-03-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Approved WMO

Date:	02-07-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	07-04-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-05-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	09-06-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2014-000455-91-NL
CCMO	NL48073.058.14