A proof of concept study on the effect of tianeptine on opioid-induced respiratory depression

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Here we will perform a proof of concept study on the ability of the antidepressant tianeptine to prevent respiratory depression from the opioid alfentanil in humans.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON40468

Source
ToetsingOnline

Brief title
STORD

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: Uit reserves opgebouwd door onderzoeksafdeling anesthesiologie

Intervention

Keyword: Opioid, Prevention, Respiratory Depression, Tianeptine

Outcome measures

Primary outcome

To assess the respiratory effects of an oral dose of tianeptine on alfentanil*

induced respiratory depression

Secondary outcome

To assess the antinociceptive effects of an oral dose of tianeptine during

alfentanil-infusion.

Study description

Background summary

Opioids induce potent analgesia but may simultaneously produce life threatening respiratory depression. Currently a number of drugs are available that prevent or reverse the respiratory effect of these potent analgesics with varying success. There is evidence that the antidepressant agent tianeptine has properties very similar to the ampakines and enhances respiratory output. Tianeptine acts at AMPA (amino*3-hydroxy-5-methyl-D-aspartate) receptors in neurons, similar to the ampakines. Glutaminergic transmission through AMPA receptors within brainstem respiratory centers, for example the pre-Botzinger complex, is essential for respiratory rhythmogenesis. Tianeptine enhances AMPA receptor-mediated transmission by acting at allosteric sites; it increases AMPA currents through kinase phosphorylation. At the same time glutamatergic transmission at NMDA receptors is reduced by tianeptine, an action very similar to that observed with the potent antidepressant ketamine, which has a tonic effect on respiration.

Study objective

Here we will perform a proof of concept study on the ability of the antidepressant tianeptine to prevent respiratory depression from the opioid alfentanil in humans.

Study design

The study will have a double blind and randomized design.

Intervention

Intravenous administration of alfentanil by target controlled infusion (set to achieve a concentration of 50 (first 8 subjects) and 100 (second group of 8 subjects) ng/ml).
Oral dose of Tianeptine (100 mg)

Study burden and risks

The study will be conducted in the anesthesiology department of a hospital, where all necessary emergency procedures are in place. The study will be conducted by researchers with experience in treating respiratory depression. Naloxone injections will be available to treat urgent, severe respiratory depression. Other support measures for breathing and hemodynamics will also be available, such as maintenance of fluids, oxygen and vasopressors. Cardiavascular emergency measures such as defibrillation, magnesium sulphate (IV) and anti-arrhytmic drugs will also be available. The overall risk/benefit assesment is considered acceptable under the conditions 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

Age of 18 to 35 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; ;Subjects using more than 20 units of alcohol per week; Use of medication during the study period;
If sexually active, the subject is not using oral 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 wellbeing 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:	Recruiting
Start date (anticipated):	04-11-2013
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Rapifen
Generic name:	Alfentanil
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tianeptine
Generic name:	Tianeptine

Ethics review

Approved WMO

Date:	23-07-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	30-09-2013

Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	17-07-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 21991
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-002974-33-NL
CCMO	NL45511.058.13
OMON	NL-OMON21991