Reversal of opioid-induced respiratory depression (OIRD) by ketamine in healthy volunteers * the ORKA trial

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

Summary

ID

NL-OMON43104

Source
ToetsingOnline

Brief title
ORKA

Condition

- Other condition

Synonym
Opioid-induced respiratory depression

Health condition

opioid-geinduceerde ademdepressie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ketamine, respiration

Outcome measures

Primary outcome

Ventilation

Secondary outcome

-

Study description

Background summary

Modern medicine relies heavily on opioids for suppression of nociception. Consequently opioids are used during anesthesia to suppress autonomic responses, during procedural sedation to reduce nociception, and given for treatment of acute (postoperative) pain and chronic pain. However, the use of opioids comes with serious side effects of which opioid-induced respiratory depression (OIRD) is most dangerous. OIRD may be related to sedation, loss of upper airway patency and central depression of rhythm generation.

There are various options to prevent or treat OIRD. We previously showed that the K+-channel blocker GAL021 effectively reverses OIRD. GAL021 is still experimental and will require many years of additional research before it may be used in clinical practice. Alternatives to GAL021 that may be used clinically are scarce. One possibility is ketamine, which is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist but interacts with many more receptor system. It is our clinical experience that ketamine is without serious respiratory events, in fact various experimental and human studies associate ketamine with respiratory stimulation. For example, in mice with a RETT syndrome phenotype, ketamine improved respiration with a reduction of the number of RETT-syndrome related apneas, which is due to either NMDA receptor or nicotinergic acetylcholine receptor antagonism. In rats, Eikermann et al. showed that ketamine stimulates breathing and activates upper airway tone. Also

human studies indicate that ketamine stimulates breathing activity. Mortero et al. showed that co-administration of ketamine with propofol significantly improved ventilation in sedated patients compared with propofol sedation only. While these data indicate that ketamine stimulates breathing there are no studies on ketamine*s effect on opioid-induced respiratory depression. Our study proposal is to investigate the effect of ketamine on respiration in healthy volunteers with suppressed breathing caused by an opioid.

Study objective

We hypothesize that ketamine stimulates breathing and reverses opioid-induced respiratory depression. We will perform a placebo-controlled randomized and double blind study on the effect of increasing doses of S-ketamine on remifentanil-induced respiratory depression in healthy male and female volunteers.

Study design

Double-Blind, randomized, placebo controlled

Intervention

Infusion of ketamine on top of a remifentanil infusion.

Study burden and risks

The burden and risk of the study are limited. The investigators have ample experience in the use of the chosen treatments and the experimental setup.

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 volunteers, aged 18 and older

Exclusion criteria

- Known or suspected neuromuscular or a (family) history of any neuromuscular disease;
- A history of allergic reaction to food or medication including study medication;
- Any current or previous medical (including high blood pressure), neurological or psychiatric illness (including a history of anxiety);
- Alcohol abuse (> 21 units/week);
- Illicit drug use in the past 30 days before inclusion;
- Pregnancy or lactation;
- Participation in any medical or drug trial in the month prior to the current study.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-10-2016
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ketamine-S
Generic name:	S(+)-ketamine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ultiva
Generic name:	remifentanil
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	01-06-2016
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Approved WMO

Date:	24-08-2016
Application type:	First submission
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	EUCTR2016-002148-17-NL
CCMO	NL57918.058.16