Reversal of morphine and morphine-6-glucuronide's respiratory effect by naloxone: A clinical study in healthy volunteers.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27397

Source
NTR

Brief title
N/A

Sponsors and support

Primary sponsor: LUMC
Source(s) of monetary or material Support: CeNeS Ltd, Cambridge UK supports part of the study

Intervention

Outcome measures

Primary outcome

Minute ventilation and pain response to heat pain.

Secondary outcome

N/A

Study description

Background summary

Morphine is partly metabolized to the active compound morphine-6-glucuronide (M6G). Both agents act through activation of the ì-opioid receptor (MOR with its subreceptors MOR1 and MOR2).
Animal studies indicate that M6G is more potent than morphine with respect to its analgesic properties while ‘anecdotal’ human studies indicate that M6G causes less obstipation, nausea, vomiting and respiratory depression.
The cause for the different side effect profile of these two opioids remains elusive, but is most probably related to either the differential affinity of morphine and M6G for the MOR2 receptor or the action of M6G at a specific M6G-receptor.
Since the late 1980’s M6G is available for experimental studies in humans and animals. After intrathecal infusion, M6G produces potent analgesia in humans.
We recently observed potent analgesia after iv M6G infusion at a dose of 20 to 30 mg/70 kg in a group of healthy volunteers.

In this study we will assess the ability of naloxone, a non-specific opioid receptor antagonist, to reverse morphine and M6G-induced respiratory depression. It is not only of clinical importance to know whether naloxone is able to reverse the most important acute side effect of these opioids (i.e., respiratory depression and apnea), but also to quantify the steady-state naloxone concentration needed to fully reverse the respiratory depression of morphine and M6G in humans.
In order to do se we will apply an adaptive trial design to identify the optimal steady-state naloxone concentration for reversal of morphine and M6G-induced respiratory depression.

We will study 4 groups, with 12 subjects per group.
- Group I will receive M6G 0.2 mg/ kg,
- Group II M6G 0.4 mg/kg,
- Group III morphine 0.15 mg/kg and finally
- Group IV morphine 0.3 mg/kg.

These opioids will be administered intravenously as bolus dose. Ninety min after the opioid infusion naloxone will be infused using a target controlled infusion system for 1-h. Next measurement will continue for another 2 hours. The opioid doses to be used are based on previous studies as well on clinical efficacy.

Study objective

This is a pharmcological study to examine the ability to reverse respiratory depression from opioids such as morphine and M6G by low dose naloxone.

Study design

N/A

Intervention

Measurement of respiration on a breath-to-breat basis.
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Contacts

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Eligibility criteria

Inclusion criteria

1. Healthy volunteers 18+.

Exclusion criteria

1. Obesity (BMI > 30);

2. Presence of medical disease (heart-, lung-, liver-, kidney-, neurological disease; diabetes m.; pyrosis; diaphragmatic hernia);

3. Presence of psychiatric disease;

4. History of chronic alcohol or drug use;

5. Allergy to study medications;

6. Possibility of pregnancy; and

7. Lactating females.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2005

Enrollment:	60
Type:	Actual

Ethics review

Positive opinion Date:	06-09-2005
Application type:	First submission

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
NTR-new	NL200
NTR-old	NTR237
Other	: N/A
ISRCTN	ISRCTN59442355

Study results

Summary results
N/A