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

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

| | |
|---|---|
| **Ethische beoordeling** | Positief advies |
| **Status** | Werving gestopt |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON27397

**Bron**
NTR

**Verkorte titel**
N/A

### Ondersteuning

**Primaire sponsor:** LUMC
**Overige ondersteuning:** CeNeS Ltd, Cambridge UK supports part of the study

### Onderzoeksproduct en/of interventie

### Uitkomstmaten

**Primaire uitkomstmaten**

Minute ventilation and pain response to heat pain.

# Toelichting onderzoek

### Achtergrond van het onderzoek

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.

### Doel van het onderzoek

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

**Onderzoeksopzet**

N/A

**Onderzoeksproduct en/of interventie**

Measurement of respiration on a breath-to-breat basis.
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- Group III morphine 0.15 mg/kg and finally
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# Contactpersonen

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## Wetenschappelijk

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# Deelname eisen

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Healthy volunteers 18+.

## Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

# Onderzoeksopzet

## Opzet

| | |
|---|---|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Parallel |
| Toewijzing: | Gerandomiseerd |
| Blindering: | Dubbelblind |
| Controle: | Placebo |

## Deelname

Nederland

| | |
|---|---|
| Status: | Werving gestopt |
| (Verwachte) startdatum: | 01-01-2005 |
| Aantal proefpersonen: | 60 |
| Type: | Werkelijke startdatum |

## Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 06-09-2005 |
| Soort: | Eerste indiening |

## Registraties

### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

| Register | ID |
|---|---|
| NTR-new | NL200 |
| NTR-old | NTR237 |
| Ander register | : N/A |
| ISRCTN | ISRCTN59442355 |

## Resultaten

**Samenvatting resultaten**
N/A