Combined effect of Pregabaline and Oxycodone, and Lacosamide and Oxycodone, on breathing: an exploratory study in healthy volunteers the POLO study

Published: 21-06-2022
Last updated: 30-01-2025

The objective of the study is to quantify the effect of pregabaline and lacosamide on oxycodone-induced respiratory depression.

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

Summary

ID

NL-OMON53730

Source
ToetsingOnline

Brief title
POLO study

Condition

- Other condition

Synonym
oxycodone-induced respiratory depression, respiratory depression

Health condition

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: Breathing, Lacosamide, Oxycodone, Pregabalin

Outcome measures

Primary outcome

Extrapolated ventilation at end-tidal PCO2 of 55 mmHg (VE55), 4-h following the

intake of oxycodone.

Secondary outcome

(1) Level of sedation; (2) Relief of nociception; (3) Occurrence of

nausea/vomiting;

(4) pupil diameter; (5) baseline ventilation.

Study description

Background summary

Opioids are commonly prescribed for moderate to severe pain. While initially intended for moderate to severe acute and cancer pain, opioids are currently frequently considered and prescribed in chronic noncancer pain. Due to the large increase in opioid prescription rate, the number of unintentional drug overdoses is rapidly increasing, not only in the Unites States but also in the Netherlands. A potential lethal consequence of an opioid overdose is opioid-induced respiratory depression. Additionally, it is well known that opioids are often used (and abused) in combination with other legal or illicit substances, for example alcohol, benzodiazepines, cannabis, neuropathic pain medication including the anticonvulsant pregabaline. There are no high-quality data on the interaction between oxycodone and (neuropathic pain) medication on the ventilatory control system. Case reports and randomized studies show that

pregabalin induces respiratory depression when combined with opioids. Some alternatives to pregabalin may have a better safety profile. One such alternative is lacosamide, an antiepileptic with a different mode of action than pregabalin, and effective in the treatment of neuropathic pain.

Study objective

The objective of the study is to quantify the effect of pregabaline and lacosamide on oxycodone-induced respiratory depression.

Study design

Double-blind, randomized cross-over design.

Intervention

Visit A: Oxycodone 10 mg tablet at t = 0 min + pregabaline 150 mg at t = 90 min;
Visit B: Oxycodone 10 mg tablet at t = 0 min + lacosamide 150 mg at t = 90 min.
Visit C (extra arm): Oxycodone 10 mg tablet at t = 0

Study burden and risks

Opioids produce several side effects, which are the topic of the current study. Gaining information on these side effects, specifically respiratory depression, especially in combination pain treatment, is of importance given the current opioid epidemic and high number of opioid toxicities in the world. Since the study is performed under highly controlled and monitored conditions, the occurrence of temporary side effects will have limited impact on the subject. During the study, we will closely monitor the subjects and treat side effects, most importantly nausea by intravenous administration of an antiemetic.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA

NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- aged 18-45 years,
- body mass index < 30 kg.m-2,
- able to understand the written informed consent form,
- able to communicate with the staff,
- able and willing to complete the study procedures,
- signed the informed consent form,

Exclusion criteria

- Presence or history of any medical or psychiatric disease (incl. a history of substance abuse, anxiety, or the presence of a painful syndrome such as fibromyalgia);
- Use of any medication in the three months prior to the study (incl. paracetamol or other pain killers);
- Use of more than 21 alcohol units per week;
- A positive urinary drug test or a breath alcohol test at screening or on the morning of the experiment;
- Pregnancy, lactating or a positive pregnancy test on the morning of the experiment;
- Participation in another drug trial in the 60 days prior to dosing.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-10-2022
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lyrica
Generic name:	Pregabalin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Oxycodone
Generic name:	Oxycodone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Vimpat
Generic name:	Lacosamide
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	21-06-2022
Application type:	First submission

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	18-07-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	06-01-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	13-01-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	20-01-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	10-02-2023
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2022-001603-40-NL
CCMO	NL81207.058.22