Alcohol and Oxycodone - The influence of the combination of alcohol and an opioid on ventilation in healthy young and elderly volunteers - the 'A&O' study

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

Summary

ID

NL-OMON40452

Source
ToetsingOnline

Brief title
A&O study

Condition

- Other condition

Synonym
Respiratory depression and reduced breathing

Health condition

Opioid geinduceerde ademhalingsdepressie

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: Alcohol, Opioid, Respiratory depression

Outcome measures

Primary outcome

A shift of the Vi*CO2 response curves measured pre-dose, during alcohol clamp,

two times after administration of oxycodone and concomitant adminstration of

alcohol and one after discontinuation of alcohol administration.

Secondary outcome

1. To assess whether sedation as measured by a VAS scale and BIS monitoring is

increased in the alcohol conditions compared to the no alcohol condition.

Study description

Background summary

Opioid use and abuse has increased over the past decades. An associated increase of opioid related mortality has been observed of which opioid induced respiratory depression is thought to be the most important cause. With increasing use of opioids the adverse events caused by concomitant use of substances influencing the pharmacokinetic and pharmacodynamic properties of opioids becomes more prevalent. In forensic literature in cases of opioid related mortality concomitant use of alcohol is described most often. In previous studies focusing on the respiratory effects of alcohol by itself no major effects on ventilation were observed. We hypothesize that the concomitant administration of an opioid and alcohol will result in a synergistic effect on ventilation. We will measure carbon dioxide ventilatory response curves in young and elderly healthy volunteers during an alcohol clamping method to

induce a pseudo steady state in blood alcohol level and after administration of one of the most prescribed opioid analgesics. The results of this study will provide further insight into opioid induced respiratory depression and the influence of concomitant alcohol use.

Study objective

In the current study we will measure ventilatory response, as assessed by ventilatory carbon dioxide responses to the administration of oxycodone during three conditions: a *low alcohol condition*, a *high alcohol condition* and a *no alcohol condition*. Furthermore the influence of alcohol on analgesia and sedation induced by oxycodone will be assessed. In order to achieve the two steady state alcohol conditions we will use a clamping method developed at the Centre for Human Drug Research (CHDR) by Zoethout et al. (33-36). The study will take place in two phases and will consist of a phase with 40 young volunteers and a phase with 40 elderly volunteers.

Study design

A single blind crossover study. The three conditions/study days will be defined as follows:
1 a high dose alcohol steady state with oral oxycodone (1.0 g L-1)
2 a low dose alcohol steady state with oral oxycodone (0.5 g L-1)
3 a placebo condition with oral oxycodone. (no alcohol infusion)

During the first phase young healthy volunteers will be included followed by the second fase in which elderly healthy volunteers will be included.

Intervention

Intravenous administration of ethanol inducing a steady state BrAC-level (at 0.5 g L-1 or at 1.0 g L-1)
Oral administration of Oxycodone 20mg IRS

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 of 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 fluid, oxygen and vasopressors. Cardiovascular emergency measures such as defibrillation, magnesium sulfate (IV) and antiarrhythmic drugs will also be available.

The overall risk / benefit assessment 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

- Healthy sybjects
- Aged 18-40 years (phase I)
- Aged 65 years or older (phase II)
- Body Mass Index 18-35 mm/kg2
- Subject is able to read and understand the written consent form, complete study related procedures and communicate with the study staff
- Healthy and free of significant abnormale findings as determined by medical history, physical examination and vital signs. For the elderly volunteers no abnormal findings for

kidney and liver function on laboratory tests.
- Subject is deemed suitable by the Investigator for inclusion in the study

Exclusion criteria

Current diagnosis or history of psychiatric disease
Current or chronic medical condition requiring the medication considered Cytochrome P-450 (CYP2E1, CYP2D6, CYP3A4) inductor or current use of opioid analgesics
Current diagnosis or history of lung disease (i.e. asthma, COPD, tuberculosis)
Exclusion based on medication use is subject to jugdment by investigators
Participation in a clinical drug study during the 60 days preceding the initial dosing of this study
Any history of frequent nausea or vomiting regardles of etiology
Weekly alcohol intake exceeding the equivalent of 21 units/week or positive alcohol breath test during check-in
Asian ethnicity

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-09-2013
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Oxycodone
Generic name:	Oxycodone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	29-07-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	11-09-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	20-11-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	18-02-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	15-04-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	12-05-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	22-05-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	24-09-2014
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-002797-42-NL
CCMO	NL45363.058.13