An explorative study to establish the panicogenic effects of a single versus double vital capacity 35% carbon dioxide inhalation challenge

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To investigate the difference in response between single and double vital capacity 35% CO2/65% O2 in terms of the occurrence of PA*s in healthy subjects as measured with the Panic Symptoms List-IV (PSL-IV) and VAS subjective anxiety and fear.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Anxiety disorders and symptoms
Study type	Observational invasive

Summary

ID

NL-OMON45528

Source
ToetsingOnline

Brief title
35% CO2 single versus double inhalation study

Condition

- Anxiety disorders and symptoms

Synonym
anxiety disorders, Panic disorders

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research

Source(s) of monetary or material Support: Centre for Human Drug Reseach

Intervention

Keyword: CO2 inhalation, Panic disorder

Outcome measures

Primary outcome

Panic attacks will be assessed by the Panic Symptoms List-IV (PSL-IV) and VAS subjective anxiety and fear.

Secondary outcome

* explore whether the occurrence of PA*s on a single vital capacity inhalation 35% CO2/65% O2 predicts occurrence of PA*s on a double vital capacity inhalation 35% CO2/65% O2.

* explore the temporal stability of the occurrence of 35% CO2/65% O2-induced PA*s in subjects who develop PA*s on a single vital capacity inhalation and subsequently receive a double vital capacity inhalation.

* explore the effects of single and double breath 35% CO2/65% O2 on heart rate, blood pressure, respiratory rate.

* explore differences in sensitivity to 35% CO2/65% O2 between male and female subjects.

Study description

Background summary

CO2 inhalation to induce panic has undergone both technical innovation and relatively extensive validation since the 1980*s.

Healthy volunteers display a concentration dependent sensitivity to inhaled CO2

while panic disorder (PD) patients consistently display the highest sensitivity to CO2, followed by first degree relatives of PD patients and healthy volunteers. In addition, registered anxiolytic drugs administered in clinically effective therapeutic doses generally have been demonstrated to reduce sensitivity CO2 in healthy volunteers and patients over time. Furthermore, the panic response to acutely inhaled CO2 remains stable and reproducible over time, tolerance does not occur after repeated administration and CO2-related carry-over effects are non-existent. Also, CO2 induces robust fear-like behaviour in preclinical models and demonstrates respiratory and cardiovascular effects that correspond to those in humans. Acute CO2 inhalation therefore represents a validated, translational fear challenge using a physiological agent which allows real-time assessment of PA*s in an experimental setting and has the potential to demonstrate panicolytic effects of novel central nervous system (CNS) active compounds in humans.

To the best of our knowledge no study has been previously published that compares single and double vital capacity 35% CO2 inhalation in a single study. Therefore, we aim to investigate the panicogenic effects of a single vs. a double vital capacity method 35% CO2 in healthy volunteers. We hypothesize that 35% CO2 double vital capacity inhalation is associated with a higher percentage of subjects experiencing a panic attack compared to single vital capacity inhalation.

Study objective

To investigate the difference in response between single and double vital capacity 35% CO2/65% O2 in terms of the occurrence of PA*s in healthy subjects as measured with the Panic Symptoms List-IV (PSL-IV) and VAS subjective anxiety and fear.

Study design

A randomized, two-way cross-over validation trial to establish the occurrence of PA*s with single and double breath 35% CO2/65% O2 vital capacity inhalation in healthy volunteers.

Study burden and risks

The acute inhalation of CO2 has been developed, validated and technically innovated over the past years as a reliable challenge model to induce an acute panic reaction that adequately resembles PAs. CO2 and O2 are harmless physiological substances that are inhaled according to a standardized challenge protocol that has been developed by Maastricht University. Numerous studies in several hundred healthy volunteers and patients suffering from panic disorder, social anxiety disorder, post-traumatic stress disorder and major depressive disorder have been conducted according to this protocol over the past 30 years.

In the majority of these studies, a mixture of 35% CO2/65% O2 had been administered as either single or double vital capacity inhalation. In all performed studies neither acute nor chronic adverse events have been reported. Also, no serious adverse events have occurred. To guarantee identical safeguards for the current study, the same absolute and relative contra-indications will be maintained and are incorporated into the in- and exclusion criteria of the protocol.

Maastricht Instruments in collaboration with Maastricht University has recently developed the CO2 tolerance tester (CTT). The CTT is a research instrument that safely and reliably induces PA*s by the protocolized administration of inhaled 35% CO2. In addition, the CTT simultaneously measures physiological changes associated with CO2-induced ANS activation such has heart rate and blood pressure. In contrast to previous experimental CO2 set ups, the CTT yields integrated real time information on ANS panic-related parameters following acute CO2 inhalation which can be readily combined with subjective assessments such as fear intensity. The CTT is particularly relevant to research in the field fear-related psychiatric disorders and is a potentially useful tool in CNS drug development with novel anxiolytic compounds.

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

1. Informed consent in writing.
2. Healthy male or female aged between 18 and 55 years (inclusive) at screening.
3. BMI of 18-32 kg/m2 (inclusive).
4. Non-smoker for at least 3 months.
5. Ability to communicate adequately with the Investigator in the Dutch language and is willing to comply with the study restrictions.

Exclusion criteria

1. Current or past history of any psychiatric disorder as classified according to DSM-IV or DSM 5.
2. Current or past history of alcohol or any substance abuse or dependence disorder within the past 12 months.
3. Presence of panic disorder as classified by DSM-IV and diagnosed by a psychiatrist or classified by the module Panic Disorder (E) of the MINI International Neuropsychiatric Interview during screening.
4. Subject drinks, on average, more than 8 cups of tea/coffee/cocoa/cola/caffeinated beverages (e.g., energy drink) per day.
5. Subject has a clinically significant acute illness within 7 days prior to the CO2 challenge.
6. Systolic blood pressure (SBP) greater than 140 or less than 90 mm Hg, and diastolic blood pressure (DBP) greater than 90 or less than 50 mm Hg
7. Clinically significant ECG abnormalities.
8. Clinically significant abnormality of the lungs (e.g. COPD, asthma, lung fibrosis) and hematologic diseases concerning hemoglobin (e.g. thalassemia and sickle cell disease).
9. Important cardiovascular history, or suspicion of infarct, cardiomyopathy, cardiac failure, TIA, angina pectoris, cardiac arrhythmias, CVA.
10. Personal or familial history of cerebral aneurysm.
11. Pregnancy as demonstrated by urine pregnancy test during screening or at each study day.
12. Use of any psychotropic drugs.
13. Have a urine drug screen detecting illicit drug of abuse (morphine, benzodiazepines, cocaine, amphetamine, THC) or a positive alcohol breath test at screening of elke studiedag

Study design

Design

Study type:	Observational invasive
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-05-2017
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	20-04-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 26851
Source: NTR

Title:

In other registers

Register	ID
CCMO	NL61306.056.17
OMON	NL-OMON26851