Feasibility and pharmacokinetics of nebulized S-ketamine inhalation in healthy adults

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Hypothesis #1 efficacyWe hypothesize that a quick onset and a good adjustability of analgesia can be achieved with inhaled ketamine.Hypothesis #2 safetyInhalation of nebulized ketamine might lead to a fast onset of analgesia, with limited adverse...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON42367

Source
ToetsingOnline

Brief title
NebuKET

Condition

- Other condition

Synonym
pain, pharmacokinetics

Health condition

pain

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: inhalation, Ketamine, Pain

Outcome measures

Primary outcome

Safety

Pharmacokinetics

Secondary outcome

Pain relief

Study description

Background summary

Traditionally, ketamine is dissolved in saline and administered intravenously or intramuscularly. However, a dozen alternative routes, such as oral, nasal and rectal administration, have been described in the need of a less resource-consuming and painless administration [5]. Intranasal ketamine is frequently used in clinic and is known to result in rapid (within 2 minutes) detectable blood concentrations with peak ketamine plasma concentrations 20-30 minutes after intranasal administration [3,4]. Ketamine-induced analgesia after intranasal application is known to correlate with plasma concentrations of both ketamine and its metabolite norketamine [4]. Intranasal ketamine administration is without overt side effects. Described adverse events are transient and similar as observed with other routes of administration. These include dizziness, nausea, feeling of unreality, sedation, and are dose-related [2,4,7]. No adverse events have been described after intranasal ketamine use that affect vital signs (such as oxygen saturation and blood pressure). Surprisingly, so far there have been no reports of ongoing (www.clinicaltrials.gov, www.clinicaltrialsregister.eu, www.umin.ac.jp/ctr/index.htm, http://www.anzctr.org.au, http://www.trialregister.nl (last checked: March 2015)) or published (Pubmed, EMbase (last checked: March 2015)) human studies that tested ketamine

administration by inhalation, with the exception of one publication. In this publication, nebulized ketamine (50 mg) was administered to postoperative patients to assess reduction of post-operative sore throat [1]. The authors describe that nebulized ketamine was tasteless, and they observed reduced post-operative sore throat in ketamine-treated patients, compared to placebo-treated patients. What is of importance is that patients in both groups remained hemodynamically stable with no nausea, vomiting, stridor, laryngospasm, cough, dry mouth, hoarseness, dissociative symptoms or any other adverse effect during the entire study period [1]. However, their primary aim was to assess topical analgesia in the throat, and they did not study systemic analgesia and/or blood pharmacokinetics. Canine data showed effective plasma levels after inhalation of nebulized ketamine (unpublished observations). For humans no pharmacological data on administration of nebulized ketamine is available. Nebulization would be a novel route for ketamine administration that is an easy and safe alternative in the treatment of acute and chronic pain and clinical depression. This would allow painless and easy administration in a huge population of patients. In the future, even at home self-application might be feasible for depressive or chronic pain patients.

Study objective

Hypothesis #1 efficacy
We hypothesize that a quick onset and a good adjustability of analgesia can be achieved with inhaled ketamine.

Hypothesis #2 safety
Inhalation of nebulized ketamine might lead to a fast onset of analgesia, with limited adverse events.

To this end, nebulized ketamine will be administered to healthy volunteers and pharmacokinetic and pharmacodynamic parameters will be measured.

Study design

Open label

Study burden and risks

Mild to moderate: psychomimetic side effects during expsoure to ketamine

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

Subjects of either sex (10 men/10 women), aged 18-39 years with a body mass index <= 30 kg/m2

Exclusion criteria

Severe medical disease including pulmonary disease, hypertension, liver/renal disease, neurological disorders, diaphragmatic hernia/pyrosis; (history of) psychiatric or neurological disease; pregnancy/lactation; allergy to study medication; (history of) illicit drug use/alcoholism; concurrent participation in another trial.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-08-2015
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ketanest S 25
Generic name:	S Ketamine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-06-2015
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	03-11-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	13-11-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2015-001601-13-NL
CCMO	NL53147.058.15