Pharmacokinetic-pharmacodynamic modeling of S(+)-ketamine in healthy volunteers.

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24166

Source
Nationaal Trial Register

Brief title
KET study.

Health condition

Healthy volunteers free of pain will be tested.

Sponsors and support

Source(s) of monetary or material Support: TREND FUND

Intervention

Outcome measures

Primary outcome

Analgesia and Plasma Cp of ketamine.

Secondary outcome

Bowdle scale parameters.

Study description

Background summary

The NMDA-receptor antagonist ketamine, at relatively low-dose, is a potent analgesic. It is used in the perioperative setting as well as in chronic pain, for example in the treatment of neuropathic pain and pain from malignancies. We are currently assessing ketamine's analgesic efficacy in CRPS type 1 patients in an experimental study (protocol P05.100).

Despite its wide use, relatively little is knows about ketamine's pharmacokinetics –PK– and pharmacodynamics –PD– or the link between the two. For example, there is no knowledge on the link parameter ke0, which is an estimate of the drugs onset and offset-times. Knowledge of ketamine's PK and PD is needed to be able to fully understand clinical ketamine data in patients, such as CRPS type 1 patients. Furthermore, it will enable the optimization of infusion schemes and hence the treatment of patients on ketamine.

Ketamine is a racemic mixture. Recently the S(+) form became available (Ketanest). In contrast to the racemic mixture, S(+)-ketamine shows less psychomimetic side effects. This is the reason that the S(+) form is now widely used with the racemic mixture rapidly loosing market.
In this study we will assess the pharmocokinetics and pharmacodynamics of intravenous S(+)-ketamine in healthy volunteers. This will result in a pharmacokinetic/pharmaco-dynamic (PK/PD) model which may be used to predict S(+)-ketamine concentration and pain relief after intravenous infusion.

The PK of S(+)-ketamine will be studied by obtaining arterial blood samples at regular times after iv infusion. The PD of S(+)-ketamine will focus on pain relief and the side effect profile, with special emphasis on psychomimetic side effects and blood pressure.

The design of the study is placebo-controlled, single-blind, randomized cross-over.

Aims of the study:

1) To obtain pharmacokinetic parameters of S(+)-ketamine;

2) To study the pharmacodynamic effects of intravenous S(+)-ketamine on experimental pain;

3) To study the pharmacodynamic effects of intravenous S(+)-ketamine using Bowdle scales.

Study objective

We will investigate the relationship between S(+)-ketamine plasmaconcentrations and its

analgesic effect to estimates the onset/offset times of ketamine and potency parameters for various analgesia tests. This will allow the safer administration of S(+) ketamine in clinical practice.

Intervention

Infusion of S(+)-ketamine or placebo.
The are three infusion schemes:
I. In four subjects there will be two 30-min infusions of S(+)-ketamine, separated by 30-min of no-infusion (end of infusion is at t = 90 min).
II. In four subjects there will be five 10-min infusions of (S)+-ketamine, all separated by 10-min of no-infusion (end-of infusion is at t = 90 min).
III. In four subjects there will be three 20-min infusions of S(+)-ketamine, all separated by 20-min of no-infusion (end of infusions is at t = 100 min).
IV. As I, but now placebo (NaCl 0.9%) will be infused.
V. As II, but now placebo (NaCl 0.9%) will be infused.
VI. As III, , but now placebo (NaCl 0.9%) will be infused.

Contacts

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Eligibility criteria

Inclusion criteria

1. Healthy volunteers 18+.

Exclusion criteria

1. Obesity (BMI > 30);
2. Presence of medical disease (heart-, lung-, liver-, kidney-, neurologic 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
Lactation.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Single blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2007
Enrollment:	24
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL636
NTR-old	NTR696
Other	: N/A
ISRCTN	ISRCTN20522161

Study results

Summary results
N/A