

# Pilot study to investigate the pharmacokinetics and tolerability of midazolam nose spray

<b>Submission date</b> 11/05/2011	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 18/05/2011	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 30/10/2015	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Epilepsy is a condition that affects the brain and causes repeated seizures. Before a drug can be given to people with epilepsy, it is necessary to know how the drug behaves in the human body. One of the first steps is to give the drug to healthy volunteers and analyze blood samples. After analyzing we can describe how the body affects a drug, including absorption (entering the blood circulation), distribution, metabolism and elimination of the drug - this is called pharmacokinetics. Doctors usually treat epileptic seizures with diazepam given through the anus, but this kind of application is not patient friendly and difficult to administer by bystanders. To find another drug to stop epileptic seizures, we need to find other drugs and ways to deliver them. Midazolam nose spray has been developed for this goal. The aim of this study is to find out about the absorption, distribution, metabolism and elimination of midazolam when administered as a nose spray compared to midazolam administered intravenously (into a vein) in healthy volunteers.

### Who can participate?

Healthy volunteers aged 18-65.

### What does the study involve?

Participants are randomly allocated to one of two groups. Participants in group 1 are treated with the midazolam nose spray, then after at least five days they are treated with intravenous midazolam.

Participants in group 2 receive the same treatments in the reverse order. In both groups blood samples are taken before administration and at regular intervals up to 240 minutes after dosing. During these 240 minutes participants inform the researcher of any adverse effects and indicate the degree of drowsiness and burning feeling in the nose.

### What are the possible benefits and risks of participating?

All treatments have side effects. The most common side effect of midazolam nose spray is drowsiness and a burning feeling in the nose.

### Where is the study run from?

Maastricht University Medical Center, the Netherlands.

When is the study starting and how long is it expected to run for?  
November 2005 to April 2006

Who is funding the study?  
Maastricht University Medical Center, the Netherlands.

Who is the main contact?  
Mrs Nicole Veldhorst

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Mrs Nicole Veldhorst

**Contact details**  
P. Debyelaan 25  
Maastricht  
Netherlands  
6229 HX

## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
N/A

## Study information

**Scientific Title**  
Pharmacokinetics and tolerability of a formulation of midazolam 50 mg/ml nose spray vs midazolam 1 mg/ml intravenously administered in healthy Dutch subjects: a single dose, randomised-sequence, open-label, two-period crossover pilot study

**Study objectives**  
To investigate pharmacokinetics and tolerability of midazolam in a new formulation, administered as a 50 mg/ml intranasal (IN) spray compared with intravenous (IV) (2.5 mg) administration in healthy adult volunteers.

**Ethics approval required**  
Old ethics approval format

**Ethics approval(s)**

**Study design**

Single-dose randomised-sequence open-label two period crossover pilot study

**Primary study design**

Interventional

**Secondary study design**

Randomised cross over trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet

**Health condition(s) or problem(s) studied**

Epileptic seizures

**Interventions**

In this cross over study subjects are randomly assigned to receive IN or IV midazolam, with a washout period of at least five days between treatments.

The 50 mg/ml IN midazolam formulation consists of 5 mg midazolam base per 0.1 ml (one spray) and is administered once in one nostril. The IV midazolam solution (2.5 mg) is infused over 10 seconds also once. Blood samples are taken before administration and at regular intervals up to 240 minutes after dosing. The duration of the intervention is 240 minutes.

**Intervention Type**

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Midazolam

**Primary outcome measure**

Pharmacokinetics of midazolam nose spray (5 mg, 50 mg/mL formulation) compared with intravenous administration (2.5 mg) - Blood samples for pharmacokinetic analysis were collected from an intravenous (IV) cannula at baseline and at 3.5, 15, 20, 30, 40, 60, 90, 120, 180 and 240 minutes post-dose. Pharmacokinetic data [maximum concentration (C<sub>max</sub>), time to maximum plasma concentration (T<sub>max</sub>), biological half life (t<sub>1/2</sub>), area under the Curve (AUC)] are analysed using two-compartment analysis.

## Secondary outcome measures

Tolerability of midazolam nose spray (50 mg/mL formulation) - Subjects are instructed to inform the investigator of any untoward effects occurring during the study, including both local adverse events and systemic adverse events. Major expected side effects, like drowsiness and local burning feeling, were registered by a Visual Analogue Scale (VAS) form 0 = no complaint at all to 100 = worst complaint possible, others were described.

## Overall study start date

01/11/2005

## Completion date

01/04/2006

# Eligibility

## Key inclusion criteria

1. Age more than or equal to 18 years, either sex
2. American Society of Anesthesiology patient classification status (ASA) I and II

## Participant type(s)

Patient

## Age group

Adult

## Lower age limit

18 Years

## Sex

Both

## Target number of participants

9

## Key exclusion criteria

1. Allergy to benzodiazepines
2. Acute or chronic nasal problems like rhinitis or sinusitis
3. Use of benzodiazepines or grapefruit was prohibited for a week prior to the research

## Date of first enrolment

01/11/2005

## Date of final enrolment

01/04/2006

# Locations

## Countries of recruitment

Netherlands

**Study participating centre**

**P. Debyelaan 25**

Maastricht

Netherlands

6229 HX

## **Sponsor information**

**Organisation**

Maastricht University Medical Centre (Netherlands)

**Sponsor details**

P.Debyelaan 25

Maastricht

Netherlands

6229 HX

**Sponsor type**

University/education

**ROR**

<https://ror.org/02d9ce178>

## **Funder(s)**

**Funder type**

University/education

**Funder Name**

Maastricht University Medical Centre (Netherlands)

## **Results and Publications**

**Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date****Individual participant data (IPD) sharing plan**

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/12/2011		Yes	No