ISRCTN79059168 https://doi.org/10.1186/ISRCTN79059168

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

Submission date
11/05/2011

Recruitment status
No longer recruiting

Registration date
18/05/2011

Overall study status
Completed

Last Edited
30/10/2015

Condition category
Nervous System Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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 describes 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

Protocol serial number
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)
Medical Ethics Committee, Maastricht University Medical Centre (MUMC), 21/02/2003, MEC-02-143.5

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

Primary study design
Interventional

Study type(s)
Treatment

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(s)
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 (Cmax), time to maximum plasma concentration (Tmax), biological half life (t1/2), area under the Curve (AUC)] are analysed using two-compartment analysis.

Key secondary outcome(s))
Tolerability of midazolam nose spray (50 mg/mL formulation) - Subjects are instructed to inform the investigator of any untoward effects occuring 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.

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Allergy to benzodiazepines
2. Acute or chronic nasal problems like rhinitis or sinusits
3. Use of benzodiazepines or grapefruit was prohibitied 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)

ROR
https://ror.org/02d9ce178

Funder(s)

Funder type
University/education

Funder Name
Maastricht University Medical Centre (Netherlands)

Results and Publications

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?
Results article	results	01/12/2011		Yes	No