

# Haloperidol Pharmacokinetics after Oral and Intravenous administration in Elderly

Published: 04-07-2016

Last updated: 16-04-2024

To obtain a nonlinear mixed effects model (NONMEM) describing the population pharmacokinetics of haloperidol in the central (CSF) and peripheral compartment after oral and intravenous injection.

<b>Ethical review</b>	Not approved
<b>Status</b>	Will not start
<b>Health condition type</b>	Deliria (incl confusion)
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON43207

### Source

ToetsingOnline

### Brief title

HOPE

### Condition

- Deliria (incl confusion)

### Synonym

acute confusional state, delirium

### Research involving

Human

### Sponsors and support

**Primary sponsor:** Kennemer Gasthuis

**Source(s) of monetary or material Support:** SAHZ en UMC Utrecht; promotiefonds

## Intervention

**Keyword:** elderly, haloperidol, pharmacokinetics

## Outcome measures

### Primary outcome

Nonlinear mixed effects model describing the population pharmacokinetics of haloperidol in the central and peripheral compartment after oral and intravenous injection.

### Secondary outcome

Occurrence of adverse events and occurrence of postoperative delirium

## Study description

### Background summary

Delirium is a common but very serious complication in post-operative elderly with long term consequences such as increased mortality, cognitive decline and institutionalisation. Prevention of delirium would be advantageous for both patients and their caregivers. Prophylactic haloperidol administration has been studied in a couple of studies obtaining mixed results. In these studies different routes of administration and haloperidol doses were used. Based on these differences in haloperidol dosing the obtained mixed results could be explained by haloperidol pharmacokinetics; the haloperidol concentration might just have been too low during the operation to obtain a protective effect. Pharmacokinetics of drugs change during aging due to changes in liver- and kidney function, fat distribution and permeability of the blood-brain barrier. As a result pharmacokinetics of healthy volunteers cannot be extrapolated to elderly. To date, however the pharmacokinetics of haloperidol in elderly are unknown. In this study the pharmacokinetics of haloperidol, administered orally and intravenously are studied to gain insight in the pharmacokinetics of haloperidol both in blood and the cerebrospinal fluid (CSF) and to establish a pharmacokinetic population model for haloperidol after intravenous and oral administration.

### Study objective

To obtain a nonlinear mixed effects model (NONMEM) describing the population

pharmacokinetics of haloperidol in the central (CSF) and peripheral compartment after oral and intravenous injection.

## **Study design**

Open randomized controlled trial

## **Intervention**

All patients will receive a single dose of 3 mg haloperidol, 10 patients will receive this by way of oral administration and 10 patients by way of intravenous injection.

## **Study burden and risks**

So far, haloperidol pharmacokinetic studies in elderly have never been done. Because the pharmacokinetics of drugs change with age due to changes in fat distribution, liver/kidney function and changes in the blood brain barrier, this study can only be performed with elderly. Also, elderly patients undergoing acute surgery e.g. hip fracture have the highest risk for developing a delirium. In other studies low dose haloperidol has been well tolerated. A total of 10 blood and 10 CSF samples will be collected within a period of 3 days. Before surgery patients will be given a spinal catheter by the anesthesiologist for spinal anesthesia and postoperative pain treatment. Patients will also be given an intravenous catheter for administration of preoperative medication. Both catheters will be removed after three days. Blood- and CSF samples will be collected through these catheters, minimizing the burden of sample collection. As infection, bleeding and neurologic injury are rare but possible serious complications, patients will be closely monitored during the study period. Following standard procedure, patients will be screened preoperatively and admitted to the hospital for the surgery and the first days following surgery. No extra site visits are necessary. Questionnaires and diaries are not part of this study.

## **Contacts**

### **Public**

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adults (18-64 years)

Elderly (65 years and older)

### Inclusion criteria

hip fracture surgery

65 years or over

DRAS score 5 or over

informed consent

### Exclusion criteria

haloperidol allergy

QTc prolongation

Parkinsons's disease

Lewy body dementia

use of anticoagulents

liver failure

## Study design

### Design

**Study type:** Interventional

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

## Recruitment

NL	
Recruitment status:	Will not start
Start date (anticipated):	01-08-2016
Enrollment:	20
Type:	Anticipated

## Medical products/devices used

Product type:	Medicine
Brand name:	Haldol
Generic name:	Haloperidol
Registration:	Yes - NL outside intended use

## Ethics review

Not approved	
Date:	30-06-2016
Application type:	First submission
Review commission:	METC Noord-Holland (Alkmaar)

## 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	EUCTR2016-000562-35-NL
CCMO	NL57305.094.16