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.

Ethical review	Not approved
Status	Will not start
Health condition type	Deliria (incl confusion)
Study type	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, fatdistribution and permeability of the blood-brain barrier. As a result pharmacokintetics 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 de 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
Kennemer Gasthuis

Boerhaavelaan 24
Haarlem 2035RC
NL
Scientific
Kennemer Gasthuis

Boerhaavelaan 24
Haarlem 2035RC
NL

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