Efficacy of haloperidol to decrease the burden of delirium in adult critically ill patients: a prospective randomised multicenter double-blind placebo-controlled clinical trial

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To assess the efficacy of haloperidol to resolve delirium in adult critically ill patients and thereby render the patient awake and non-delirious.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Deliria (incl confusion)
Study type	Interventional

Summary

ID

NL-OMON48650

Source
ToetsingOnline

Brief title
Haloperidol for delirium in critically ill patients

Condition

- Deliria (incl confusion)

Synonym
acute brain-dysfunction, confusion

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Critical Care, Delirium, Haloperidol, Outcome Assessment (Health Care)

Outcome measures

Primary outcome

Delirium- and coma free days at ICU [up to 14 days after randomisation].

Secondary outcome

To study the efficacy of haloperidol to reduce ICU-delirium associated short- and long-term burdens (up to one-year), consisting of: 1) mortality; 2) cognitive and functional impairment; 3) patient- and family experiences and psychological sequelae during and after ICU stay; 4) safety concerns associated with haloperidol use.

Study description

Background summary

Delirium in critically ill patients is associated with a threefold increase in mortality risk and delirium duration strongly correlates with cognitive decline after intensive care unit (ICU) stay. Authoritative evidence-based guidelines (2013) on integrated pain, agitation and delirium (PAD) management have therefore proposed to perform screening for delirium symptoms in all critically ill patients and implement multiple preventive measures for delirium. These guidelines highlighted the evidence indicating the need for early awakening of critically ill patients by using less sedation, early as possible trials to remove the endotracheal tube, active vigilance, prevention and management of delirium and early mobilisation to effectively reduce both the burdens associated with delirium and the chance of poor outcomes. These PAD guidelines and several national (Dutch) guidelines on (ICU) delirium have indicated that there are no adequately powered trials on efficacy of haloperidol for the

treatment of ICU delirium and associated adverse outcomes.

Study objective

To assess the efficacy of haloperidol to resolve delirium in adult critically ill patients and thereby render the patient awake and non-delirious.

Study design

Prospective, multicentre, double-blind placebo-controlled randomized intervention study.

Intervention

Haloperidol versus placebo in delirious critically ill patients starting with 2.5mg IV q8h and titrated to maximum 5mg IV q8h.

Study burden and risks

The burden associated with participation will include cognitive, functional and psychological assessments at 3 and 12 months. The associated risk of participation is estimated to be negligible, since the study drug is already common practice and surveillance will due to study procedures increase, enhancing rather then impeding safety in relation to the study drug.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Inclusion criteria for eligibility:
1. Age >= 18 years
2. Admitted to one of six participating ICUs of the EuRIDICE trial.;Inclusion criteria for randomisation:
1. Delirium, as assessed with the Intensive Care Delirium Screening Checklist - ICDSC: >=4 or Confusion Assessment Method for the ICU - CAM-ICU: positive). NB Delirium can occur in the course of ICU admission or be present at admission.
2. Written Informed Consent is obtained from patient or legal representative
3. Complies with inclusion criteria but NOT exclusion criteria for eligibility (See above and exclusion criteria)

Exclusion criteria

Exclusion criteria for eligibility:
1. Admitted to ICU with a neurological diagnosis (such as acute stroke, traumatic brain injury, intracranial malignancy, anoxic coma). Previous non-acute stroke or other previous neurological condition without cognitive deterioration is not an exclusion criterion.
2. Pregnancy (to be excluded by pregnancy test in women of child baring age)
3. History of ventricular arrhythmia including *torsade de pointes* (TdP)
4. Known allergy to haloperidol
5. History of dementia or an Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) score >= 4
6. History of malignant neuroleptic syndrome or parkinsonism (either Parkinson*s disease or another hypokinetic rigid syndrome)
7. Schizophrenia
8. Inability to conduct valid delirium screening assessment (e.g. coma, deaf, blind) or inability to speak Dutch
9. The patient is expected to die within 24 hours, or is expected to leave the ICU within 24 hours after evaluation (may be reassessed daily);Exclusion criteria for randomisation:
1. Prolonged QT-interval (QTc > 500ms)
2. (recent) *torsade de pointes* (TdP)

3. (recent) malignant neuroleptic syndrome or parkinsonism
4. Evidence of acute alcohol (or substance) withdrawal requiring pharmacological intervention (e.g. benzodiazepines or alfa-2 agonist) to treat
5. IQCODE not assessed in patients >= 50 years old or with possible cognitive deterioration
6. The patient is expected to die within 24 hours.
7. No (previously) signed informed consent by patient or representative
8. Current participation in another intervention trial that is evaluating a medication, device or behavioural intervention

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-02-2018
Enrollment:	742
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	04-10-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-02-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-01-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-05-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 26510
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2017-003115-20-NL
CCMO	NL62689.078.17
OMON	NL-OMON26510