Randomised trial of haloperidol for delirium in critically ill patients

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26510

Source
NTR

Brief title
EuRIDICE

Health condition

Delirium, delier

Sponsors and support

Primary sponsor: Erasmus Medical Center, Rotterdam, The Netherlands
Source(s) of monetary or material Support: ZonMw

Intervention

Outcome measures

Primary outcome

Delirium- and coma free days at ICU (up to 14 days after randomisation).

Secondary outcome

1) 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.

2) Safety concerns associated with haloperidol use.

Study description

Background summary

Introduction: 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 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.

Methods and analysis: A prospective, multicentre, double-blind placebo-controlled randomised intervention study comparing haloperidol versus placebo in delirious critically ill patients, starting with 2.5mg IV q8h and titrated to a maximum of 5mg IV q8h. A total of 742 delirious patients will be recruited from six participating ICUs in the Rotterdam area in the Netherlands, excluding patients with a primary neurological diagnosis. Delirium will be assessed by the Intensive Care Delirium Screening Checklist (ICDSC) or Confusion Assessment Method for the ICU (CAM-ICU). The primary outcome will be delirium- and coma free days during ICU stay (up to 14 days after randomisation). The sample size provides power to detect a true treatment difference of one day for the primary outcome between trial arms. Secondary outcomes include 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. In addition safety concerns associated with haloperidol use will be studied and a cost-effectiveness analysis performed.

This randomised multicentre study is expected to provide evidence on the efficacy and safety of haloperidol for the treatment of ICU delirium and its associated burden. Enrollment will start in December 2017. The inclusion period will take 1.5 years, with each patient being followed for up to one year. The end of the study is defined as the last patient’s last visit.

Study objective

Our primary hypothesis is that treatment with haloperidol will result in more days alive without delirium or coma during the study period of 14 days. Secondary outcomes are related to delirium and include: mortality, cognitive and functional outcomes, and patient and family well-being, experiences associated with ICU delirium and psychological sequelae.

Study design

- Delirium-free and coma-free days. Timepoint: the first 14 days after randomisation.

- Mortality at 28 days and 1 year after hospital discharge

- Cognitive functioning at 3 and 12 months after hospital discharge

- Functional outcomes at 3 and 12 months after hospital discharge

- Cost effectivity questionnaires at 1, 3, 6 and 12 months after hospital discharge

- Questionnaires regarding patient and family experiences and wellbeing at discharge from hospital and 3 months after discharge.

Intervention

The intervention group will receive haloperidol, a butyrophenone-derived anti-psychotic with mainly dopamine-2 receptor antagonistic properties. Placebo consists of lactic acid and water for injection.

Contacts

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Eligibility criteria

Inclusion criteria

Inclusion criteria for eligibility

1. Age ≥ 18 years

2. Admitted to ICU.

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

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 or other psychotic disorder

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

6. The patient is expected to die within 24 hours, or is expected to leave the ICU 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 type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Placebo

Recruitment

NL

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

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	29-09-2017
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 48650
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL6537
NTR-old	NTR6725
CCMO	NL62689.078.17
OMON	NL-OMON48650

Study results