Rivastigmine for delirium in Intensive Care patients, a double-blind, randomised, placebo-controlled, multi-center add-on trial

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To study whether rivastigmine added to treatment with haloperidol shortens the duration of delirium in ICU patients and reduces costs.

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

Summary

ID

NL-OMON33892

Source
ToetsingOnline

Brief title
Rivastigmine for ICU-delirium

Condition

- Deliria (incl confusion)

Synonym
agitation, ICU-pyschosis, ICU-syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMw subsidie in het kader van het

programma "Doelmatigheidsonderzoek".,Novartis,Novartis levert de studie medicatie

Intervention

Keyword: Cholinesterase inhibitors, Delirium, ICU, Rivastigmine

Outcome measures

Primary outcome

Duration of delirium during hospital admission (i.e. at the ICU and at the ward combined). This will be assessed by the sum of the duration of ICU delirium (defined as the number of hours that the CAM-ICU is positive), and the duration of delirium at a ward with lower level of care (defined as the number of hours that the CAM is positive).

Secondary outcome

1. Severity of delirium as assessed with the DSI. 2. The number of times rescue medication is given in case of severe agitation, as well as the total dose of haloperidol and propofol. 3. The number and type of accidentally removed catheters. 4. Use of physical restraints. 5. Frequency and distribution of possible adverse effects. 6. Length of ICU stay.

7. The number of re-admissions to the ICU during hospital stay. 8. Length of hospital stay.

9. Cumulative survival from inclusion in the trial until 90 days. 10. Activities of daily living 90 days after inclusion in the trial. 11. Quality of life 90 days after inclusion in the proposed study. 12. Cognitive function 90 days after inclusion in the trial.

Study description

Background summary

Delirium in the Intensive Care Unit (ICU) is a frequent disorder. It is estimated that 70% of the patients in the ICU, will suffer an episode of delirium during their stay in the ICU. Delirium in the ICU is not only an unpleasant and freighting experience for the patient and their relatives, delirium is also associated with worse prognosis (higher morbidity and mortality) and higher costs. Diagnosing delirium in the ICU is a difficult task, due to the frequent inability to communicate (i.e. intubation). In this study a validated method will be used: the Confusion Assessment Method for the ICU (CAM-ICU), a method with high sensitivity and specificity. The current therapy for (ICU-) delirium is treatment of the underlying condition (e.g. urinary tract infection) and symptomatic treatment with haloperidol. Several publications and clinical experience of the investigators have shown that rivastigmine (a cholinesterase inhibitor) may have a positive effect on the duration of delirium in delirious patients.

Study objective

To study whether rivastigmine added to treatment with haloperidol shortens the duration of delirium in ICU patients and reduces costs.

Study design

Multicentre, double-blind, randomized, placebo-controlled, add-on trial.

Intervention

Delirious patients will receive the usual treatment (haloperidol). Subjects will be randomized between two groups: the intervention group and the placebo group.
Intervention group: 1,5 mg. rivastigmine twice daily. This dosage will be increased every three days with 3 mg a day, until the CAM-ICU is negative or until the occurrence of presumed severe adverse effects or until a maximum of 12 mg a day is reached.
Placebo group: twice a day, same dosage scheme as above.

Study burden and risks

Burden: Evaluation of the cognitive functions of the participants (using the CAM-ICU) will be conducted as part of the daily practice. Fur study purposes only; the participant (and the legal representative) will be assessed at base line (duration: 10 minutes), and 90 days after inclusion for among others ADL

and QoL (duration: 20 minutes).
Risk: Participants are at risk of being treated with a drug, not-indicated for their disorder. This drug (rivastigmine) however is extensively tested on humans, and the investigators of this study have extensive clinical experience with *off label* prescription of this medication for delirium. Several publications indicate that rivastigmine might have a positive effect on the duration of delirium.
Benefit: Participants may be treated with a medication of which the experts believe that it will positively affect the prognosis.
Consideration: The investigators of this study believe that the burden and risk do not exceed the benefit.

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

1. 18 years or older
2. Positive CAM-ICU
3. Anticipated ICU and/or Medium Care length of stay >48 hours

Exclusion criteria

1. Known allergy to rivastigmine
2. Unable to receive enteric medication
3. Pregnant or lactating
4. Renal replacement therapy
5. Hepatic encephalopathy
6. Second or third degree atrioventricular block
7. Uncertainty about diagnosis delirium and no confirmation by neurologist, psychiatrist or geriatrician
8. Bradycardia with hemodynamic consequences (without functioning pacemaker)
9. No informed consent

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:	Recruitment stopped
Start date (anticipated):	10-11-2008
Enrollment:	440
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	20-05-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	27-05-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-02-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-03-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	30-06-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-07-2009
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-12-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	30-12-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	03-02-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-03-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-04-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2007-005300-41-NL
ClinicalTrials.gov	NCT00704301
CCMO	NL19821.041.08