Sodium-oxybate as a potential new treatment for catatonia in patients with depression, bipolar disorder or a psychotic disorder, a randomized controlled trial. The Laborit study.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56950

Source
ToetsingOnline

Brief title
Laborit study

Condition

- Other condition
- Psychiatric disorders NEC

Synonym
Catatonia, syndrome associated with psychomotor disturbances, with either a retarded or excited nature

Health condition

Katatonie

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Nederlandse hersenstichting

Intervention

Keyword: Catatonia, ECT, Lorazepam, Sodium-oxybate

Outcome measures

Primary outcome

We will use logistic regression, to assess the response rate after 4 days of treatment between groups.

Secondary outcome

1) To determine remission of catatonia, by comparing remission to either high dose of lorazepam or sodium oxybate, after 10 days of treatment. We will only determine remission in patients who responder after 4 day of treatment with either lorazpam or sodium oxybate..

2) To determine which side effects occur if sodium oxybate is administered in patients with catatonia, with an emphasis on oxygen levels, blood pressure, heart rate and vomiting, i.e. with regard to the risk to develop aspiration pneumonia.

Study description

Background summary

Rationale: Catatonia is a severe syndrome in patients with depressive-, bipolar- and psychotic disorders. Untreated catatonia has a mortality of 10% and results in increased morbidity; renal failure, rhabdomyolysis, pneumonia, embolism and contractures. Novel therapies are needed for patients with catatonia. Currently, the only pharmacological treatment option for catatonia consists of high dose of lorazepam, a benzodiazepine and gamma-aminobutyric acid (GABA)-A receptor agonist. When lorazepam fails (in 25% of the patients), the only remaining treatment is electroconvulsive therapy (ECT). Many patients and their caregivers are reluctant to receive ECT, because of its *intrusive* nature and because of its cognitive side effects. However, most accept ECT because currently no other treatment is available.
ECT is probably successful in catatonia because it causes a huge increase in GABA levels and GABA-B function2. This has raised the question whether alternative routes of GABAergic modulation represent a novel treatment option. One observational study showed efficacy of sodium oxybate in patients with catatonia. We hypothesize that sodium oxybate is an alternative to ECT, since it is a precursor of GABA and acts as GABA-B receptor agonist. Such a pharmacodynamic profile is expected to increase GABA mediated neurotransmission levels in the brain, and is thus beneficial to patients with catatonia.

Hypothesis: Is sodium oxybate effective in psychiatric patients with catatonia, admitted to an acute psychiatric ward, who are resistant to prior treatment with lorazepam?

Study objective

This study has been transitioned to CTIS with ID 2024-517805-10-01 check the CTIS register for the current data.

We aim to investigate whether sodium oxybate can be used as a novel treatment in psychiatric patients with catatonia.
Our primary objective is: To determine if sodium oxybate is effective as a novel treatment in psychiatric patients with catatonia who are resistant to lorazepam, in a randomized controlled trial. This is obtained by comparing response to either high dose of lorazepam or sodium oxybate, after 4 days of treatment.
Our secondary objectives are:
1) To determine remission of catatonia, by comparing remission to either high dose of lorazepam or sodium oxybate, after 10 days of treatment. 2) To determine which side effects occur if sodium oxybate is administered in patients with catatonia, with an emphasis on oxygen levels, blood pressure, heart rate and vomiting, i.e. with regard to the risk to develop aspiration pneumonia.

Study design

The Laborit study combines a multicenter, prospective cohort study on patients with catatonia, admitted to a psychiatric hospital with an embedded randomized, controlled superiority trial to examine the effect of sodium oxybate on catatonia.
1) Patients with catatonia will receive care as usual: they will be titrated to a high dosage of lorazepam in 4 days, until response of catatonia symptoms occurs.
2) If no response occurs, patients will be randomized between continuation of high dose of lorazepam (n=21) for an additional 4 days or sodium oxybate (n=21) for 4 days.

The cohort provides the basis for recruitment of patients for the RCT, since in patients with catatonia there is only a limited timeframe to determine whether the next and final step (ECT) in the treatment protocol should be taken. The timeframe to decide is limited since the morbidity and mortality of catatonia is high. The cohort additionally provides an excellent opportunity to describe clinical characteristics and course of patients with catatonia and identify putative determinants.

Intervention

1) Patients with catatonia will receive care as usual: they will be titrated to a dosage of lorazepam up to 24mg daily in 4 days, until response of catatonia symptoms occurs.
2) If no response occurs, patients will be randomized between continuation of high dose of lorazepam (n=21) for an additional 4 days or sodium oxybate (n=21) for 4 days.

Study burden and risks

Benefits: Novel treatments for catatonia are necessary, since currently there are only two options, first administration of high dose lorazepam, during 4 days to 7 days and 2) if this fails ECT. This study could -if successful- contribute to a less invasive treatment with sodium oxybate in patients with catatonia who do not respond to lorazepam.
On a participant level, there might be a potential beneficial effect in those allocated to sodium oxybate.
Burden: Total time for participants ranges between 4 and 10 days. 4 days for those who do not respond to treatment and 10 days for those who do respond to treatment with sodium oxybate.
Risk: Sodium oxybate can produce deep sedation, nausea and dizziness4. Overdosage can result in respiratory depression. Co-administration with benzodiazepines increases risk for impaired consciousness and respiratory depression. Safety is of the utmost importance for this study, therefore patients will be monitored continuously when they start sodium oxybate for the first four days. Anaesthesia technicians, capable of treating respiratory

depression, having access to oxygen and a crash cart and able to intubate patients, will be assigned to observe the patients continuously. Apart from these anaesthesia technicians, patients will receive normal care from psychiatric nurses at the psychiatric wards.

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

-Patients (age 18-80) with catatonia
-With DSM-5 diagnosis of either unipolar depression, bipolar disorder, or a psychotic disorder admitted to an acute psychiatric ward.
-No response to usual care, with increasing doses of lorazepam to a maximum of 24 mg during 4 days.
-Presence of catatonia will be assessed using the BFCTRS(15). Catatonia is

considered present with a score of two or higher on the BFCTRS.
-Catatonia is present for a maximum of eight weeks.

Exclusion criteria

-Somatic disorder underlying catatonia.
-Use of anti-psychotic drugs.
-Known heart failure or renal impairment due to signifcant amounts of sodium in the sodium-oxybate.
-Known sleep apnea.
-Use of Gabaergic drugs including gabapentin or pregabalin or clonidine. Or us of valproate.
-Presence of alcohol use disorder
-Presence of malignant catatonia or development of catatonia during the study, i.e. those with malignant catatonia will be treated immediately with ECT

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2024
Enrollment:	42
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Xyrem
Generic name:	Sodium oxybate
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	22-05-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-11-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-07-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EU-CTR	CTIS2024-517805-10-01
EudraCT	EUCTR2021-004049-19-NL
CCMO	NL77938.018.24