Metabolic differences between narcoleptic patients and healthy controls, and the effect of sodium oxybate in patients

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1. To compare energy expenditure in detail between narcolepsy patients and healthy controls. 2. To compare insulin sensitivity between patients with narcolepsy and healthy controls.3. To establish the impact of chronic sodium oxybate treatment (3-4…

Ethical review	Approved WMO
Status	Pending
Health condition type	Sleep disturbances (incl subtypes)
Study type	Observational invasive

Summary

ID

NL-OMON31397

Source
ToetsingOnline

Brief title
Metabolism and Sodium Oxybate in Narcolepsy

Condition

- Sleep disturbances (incl subtypes)

Synonym
Narcolepsy

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: UCB pharma

Intervention

Keyword: Energy Expenditure, Insulin Sensitivity, Narcolepsy, Sodium Oxybate

Outcome measures

Primary outcome

1. Is there difference in energy expenditure between narcolepsy patients and

healthy

controls?

2. Is there difference in insulin sensitivity between patients with narcolepsy

and healthy controls?

3. What is the impact of chronic sodium oxybate treatment (3-4 months) on these

(above)

metabolic features in hypocretin-deficient narcoleptic patients?

Secondary outcome

not applicable

Study description

Background summary

Narcolepsy is a debilitating sleep disorder, with an estimated prevalence of 5-6 per 10,000 in the Western population.1,2 It primarily affects the organization and regulation of sleep and wakefulness. The main symptoms are excessive daytime sleepiness, cataplexy (a sudden muscle weakness triggered by emotions), and fragmented nocturnal sleep. Less explored symptoms include impaired vigilance and memory impairments.

In 1999, deficiencies in hypocretin neurotransmission were shown to be the fundamental cause of narcolepsy. Animal data showed that the hypocretin system is not only involved in sleep regulation, but also in the regulation of various hormonal ensembles and (sympathetic) autonomic nervous system functions.3,4

These findings prompted additionial research into additional symptoms in human narcolepsy. Indeed, obesity and hormonal alterations have now been identified as important and prevalent features of the disease.5-9 Why narcoleptic patients grow obese is not known. The occurrence of daytime sleep is not a sufficient explanation, and 24-hour caloric intake in narcoleptics seems to be even lower compared to healthy controls.10 At this point, the most likely explanation is a decreased sympathetic tone with a resulting decrease in energy expenditure. However, this has not been proven yet

Study objective

1. To compare energy expenditure in detail between narcolepsy patients and healthy
controls.

2. To compare insulin sensitivity between patients with narcolepsy and healthy controls.

3. To establish the impact of chronic sodium oxybate treatment (3-4 months) on these
metabolic features in hypocretin-deficient narcoleptic patients.

Study design

Total and resting energy expenditure, fuel oxidation and insulin sensitivity will be measured in all subjects at baseline by respiration chamber, indirect calorimetry, doubly-labeled water and hyperinsulinemic euglycemic clamp, respectively.
After these measurements, the narcoleptic patients will be treated with sodium oxybate for 3 months by their own neurologist. If this treatment is succesfull, all parameters will be assessed again in these patients.
In the healthy controls only the parameters on energy expenditure will be repeatedly assessed to take into account the seasonal influence. This will be done three months after the first assessment.

Study burden and risks

Participation takes time and some discomfort. Introduction of the iv's may hurt a bit and give a haematoma.
Isotopes are stable non-radioactive, and also non-toxic in the doses used.

During the hyperinsulinemic euglycemic clamp procedure serum glucose levels will be determined every 5 minutes and, if necessary, the glucose infusion rate will be adapted so the chance of hypoglycemia is very low. The isotopes used during the clamp procedure are non- radioactive and no side effects will be expected.

During the admissions at the hospital there will be a restriction of movement freedom. The only problem that may be expected is in case of claustrophobia. Subjects with claustrophobia won't be included so no problem will be expected.

Narcolepstic patients who have to stop sodium oxybate can experience a slow return of their complaints. This will be evaluated by their own physician.

Participants will receive ¤375,- (healthy controls ¤300,-)

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

-male and age between 18 and 65 years.
- Patients: sporadic narcolepsy with cataplexy (according to ICSD-2 criteria), undetectable hypocretin-1 levels in the CSF.
- Eligible for sodium oxybate treatment

Exclusion criteria

- hypertension (BP systolic > 165 or diastolic > 95 mm Hg)
- any (history of) pituitary, psychiatric or neurological disease
- diabetes mellitus (fasting plasma glucose > 6.9 mm/l)
- alcohol /drug abuse
- anemia

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2008
Enrollment:	16
Type:	Anticipated

Ethics review

Approved WMO
Application type: First submission

Review commission: METC Leids Universitair Medisch Centrum (Leiden)

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
CCMO	NL18494.058.07