Control of breathing in systemic sclerosis

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-To assess the central chemosensitivity by an carbon dioxide rebreathing test-To assess mouth occlusion pressures during the carbon dioxide rebreathing test-To study the relation between these results and the results obtained with the MRI and...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Connective tissue disorders (excl congenital)
Study type	Observational non invasive

Summary

ID

NL-OMON39967

Source
ToetsingOnline

Brief title
COB in SSc

Condition

- Connective tissue disorders (excl congenital)
- Thoracic disorders (excl lung and pleura)

Synonym
"skin sclerosis", systemic sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: hyperoxic ventilatory response to hypercapnia, mouth occlusion pressures

Outcome measures

Primary outcome

1. Hyperoxic ventilatory response to hypercapnia

2. Mouth occlusion pressures

Secondary outcome

Not applicable

Study description

Background summary

Systemic sclerosis (SSc) is a rare, systemic connective tissue disease characterized by widespread microvascular damage and by increased production and deposition of extracellular matrix components both in the skin and internal organs. Autoimmune serological abnormalities and autoantibodies production are common and the clinical presentation can differ widely for the extent and localization of visceral damage (Black CM et al. 1993, Anderson N et al. 2002). The involvement of the nervous system is usually limited and more often localized in peripheral structures (Gordon RM et al. 1970). The unusual occurrence of cerebral lesions has previously been interpreted as a complication of microvessel defects in the presence of hypertension or renal failure, or linked to antiphospholipid immunity or vasculitis (Averbuch-Heller L et al 1992; Patahak R et al 1991).

In a recent study, macro- and micro-angiopathy was shown in brains of 16 patients with limited and diffuse asymptomatic SSc by using transcranial Doppler ultrasonography (Giuliodori G et al 2009). This is a non-invasive method to measure continuously the mean flow velocity in the middle cerebral arteries. Using another imaging modality, brain MRI, hyperintensive lesions (white matter abnormalities) were detected, including the brain stem, in limited and diffuse SSc patients (Sardanelli F et al 2005; Mohamed RH et al 2010). In addition, Terrier and coworkers found an association between cerebral vasculopathy and ischemic events in patients with limited and diffuse SSc (Terrier B et al 2009).

In SSc, hypercapnic respiratory failure involves several factors (Nageh TT et al 1998; Pugazhenthi et al 2003). First, it has been suggested that an inability of respiratory muscles to sustain tension can develop as increased respiratory resistance due to skin involvement of the thorax. Second, a gradual

down-regulation in cerebral central respiratory sensitivity for carbon dioxide may occur as a result of slightly chronic elevated arterial partial carbon dioxide pressure or a high normal partial carbon dioxide pressure. However, the contribution of central and peripheral chemoreceptors, which regulate carbon dioxide levels in a negative feedback loop, to hypercapnic respiratory failure in these patients is unknown.

The normal ventilatory response to carbon dioxide is mediated by central and peripheral chemoreflexes with chemoreceptors located in the carotid and aortic bodies and the ventral medulla (Dejours P 1962). Many factors influence the chemoreceptor response and thereby the control of breathing (Patrick J 1972). To measure the ventilatory response to carbon dioxide and thereby estimating the sensitivity to carbon dioxide a rebreathing method can be used (Read DJC 1967).

In daily care for our patients with SSc, we experienced several cases of intercurrent hypercapnic respiratory failure, without known interstitial lung disease or impaired diaphragm function. In our view, carbon dioxide retention in these patients could not just be explained by a pneumonia or heart failure. In these patients the central chemoreflex drive could be involved and altered in the course of the disease. In addition, we speculate that the occurrence of cerebrovascular lesions in the brain stem may be related to an altered response of central chemoreceptors (Sardanelli F et al 2005; Mohamed RH et al 2010).

Recently, a study on the relation between neuropsychocological disorders and chronic inflammation in cerebral metabolism in systemic sclerosis started in the Leiden University Medical Center (P11.148). Apart from various questionnaires, a brain MRI including the brain stem will be obtained.

Based on the above we hypothesized that the central chemosensitivity is altered in patients with systemic sclerosis and neuropsychological disorders and is associated with the presence of hyperintensive lesions (white matter abnormalities) as is shown previously in systemic sclerosis.

Therefore we aim to investigate the respiratory drive by assessing the central chemosensitivity and measurements of mouth occlusion pressures in all patients participating in the P11.148 study.

Study objective

-To assess the central chemosensitivity by an carbon dioxide rebreathing test
-To assess mouth occlusion pressures during the carbon dioxide rebreathing test
-To study the relation between these results and the results obtained with the MRI and neuropsychological questionnaires (protocol P11.148)

Study design

Patients who participated in the MRI study (protocol P11.148) will be invited to participate in the present study. This is a cross-sectional, explorative, single center
case control study to assess the respiratory drive. Partners of patients with systemic sclerosis will be invited to the present study as healthy matched controls.

Study burden and risks

Participation will include 60 minutes of lung function measurements. Possible side effect of the measurements could be a light headiness, diminishing in a few minutes.

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:
a.age over 18 years
b.a diagnosis of SSC confirmed by criteria of the American Rheumatology Association (ACR criteria 1987)
c.participated in the MRI study (protocol number P11.148);Healthy adult controls:
a. age above 18 years

Exclusion criteria

Patients:
a. severe left-sided heart failure
b.active psychiater-diagnosed mental disorder, thereby not able to provide informed consent
c.clinical suspicion on current or recent vascular cerebral accident.;Healthy adult controls:
a. no history or symptoms/signs of disease

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-02-2013
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	23-01-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	09-10-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL42469.058.12