SARS-CoV-2 presence in the cerebrospinal fluid of COVID-19 patients with acute respiratory failure: a pilot study.

Published: 30-04-2020
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Primary objective: To investigate the prevalence of SARS-CoV-2 presence in the cerebrospinal fluid (CSF) of patients with a proven SARS-CoV-2 infection and acute respiratory failure.Secondary objectives: 1. To correlate the presence of SARS-CoV-2 in...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON49509

Source
ToetsingOnline

Brief title
Neuroinvasion in COVID-19

Condition

- Viral infectious disorders
- Central nervous system infections and inflammations

Synonym
coronavirus, COVID-19

Research involving
Human

Sponsors and support

Primary sponsor: Zuyderland Medisch Centrum
Source(s) of monetary or material Support: Mogelijk via ZonMW;subsidie-aanvraag is lopende.,Zuyderland Medisch Centrum

Intervention

Keyword: Cerebrospinal Fluid, COVID-19, Neuroinvasion, SARS-CoV-2

Outcome measures

Primary outcome

SARS-CoV-2 RT-PCR of cerebrospinal fluid (positive/negative)

Secondary outcome

Clinical characteristics

- 8-week mortality

Biochemistry and cell count of the cerebrospinal fluid

- Leukocyte count of the cerebrospinal fluid, including differential count

Biochemistry and cell count of serum

- Leukocyte count

- C-reactive protein (CRP)

- Lactate dehydrogenase (LDH)

- D-Dimer

Study description

Background summary

COVID-19 is caused by the SARS-CoV-2 virus, which shares 79% homology with the SARS-CoV virus, known for the SARS epidemic in 2002/2003. (Wu 2020) Both viruses are a member of the coronavirus subfamily. (Wu 2020) The clinical presentation of COVID-19 and SARS show a lot of similarities. Both viruses

cause a viral pneumonia with the most frequent symptoms being fever, coughing, dyspnoea, myalgia and fatigue. (Huang 2020; Hui 2003)

Typically, a COVID-19 patient will show mild symptoms for several days, after which the disease either is self-limiting, or evolves into acute respiratory failure. (Huang 2020) As of yet, the pathophysiology of this last symptom has not been fully uncovered. Neuroinvasion may play a key part, as it is a known characteristic of coronaviruses. (Desforges 2014) The presence of SARS-CoV in the brain has been proven by autopsy, although the studies did not specify from what part of the brain the biopsies were taken. (Hui 2003; Gu 2005) Research in mice primarily showed the brain stem being affected by infection of SARS-CoV, sometimes before demonstrable pulmonary involvement. (McCray 2007, Netland 2005) In one case report, SARS-CoV was detected in the cerebrospinal fluid of a patient with neurologic symptoms. (Hung et al 2003) On the basis of these findings it was hypothesised by Li 2020 and later by Baig 2020 that SARS-CoV-2 might also migrate to the brain.

Study objective

Primary objective: To investigate the prevalence of SARS-CoV-2 presence in the cerebrospinal fluid (CSF) of patients with a proven SARS-CoV-2 infection and acute respiratory failure.

Secondary objectives:
1. To correlate the presence of SARS-CoV-2 in the CSF with routine biochemistry of serum and CSF.
2. To correlate the presence of SARS-CoV-2 in the CSF to clinical presentation.
3. To correlate the presence of SARS-CoV-2 in the CSF to 8-week mortality.
4. To investigate the presence of abnormalities in routine CSF biochemistry in patients with a proven SARS-CoV-2 infection and acute respiratory failure.

Study design

Single-centre pilot study

Study burden and risks

All patients will be exposed to the complications and discomfort associated with diagnostic lumbar puncture, which is considered a low-risk procedure. As patients will be sedated during the procedure, they will not experience periprocedural discomfort. The study is considered group-related as uncovering the pathophysiology of acute respiratory distress in COVID-19 patients may be a starting point for research aimed at improving the prognosis of COVID-19 patients.

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

- At least 18 years of age
- Requires mechanical ventilation
- Proven SARS-CoV-2 infection
- Lumbar puncture possible within 48 hours of ICU admission
- Informed consent provided by either patient or legal representative

Exclusion criteria

- Any contraindication for lumbar puncture
- Proven or suspected cerebrospinal fluid leak or other blood-brain barrier defects

- Any condition known to alter cerebrospinal fluid biochemistry
- Known or suspected cause for respiratory failure, other than COVID-19
- Any disease known for decreasing pulmonary capacity or compliance

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO

Date:	30-04-2020
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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	NL73739.096.20