Hospital Employees Response Ante COVID-19 Listed Early Symptoms (HERACLES): A clinical study to examine the dynamics of the host-response to viral infection including COVID-19 in healthcare workers

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON49285

Source
ToetsingOnline

Brief title
HERACLES

Condition

- Viral infectious disorders

Synonym
coronavirus infection, COVID-19 infection

Research involving

Human

Sponsors and support

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

Intervention

Keyword: COVID-19, healthcare workers, viral infection

Outcome measures

Primary outcome

Primary Objective

To determine the diagnostic accuracy of TRAIL and/or IP-10 for detection of viral infections including COVID-19 during the pre-symptomatic phase in healthcare workers at increased risk for respiratory viral infection.

Primary Endpoint

Sensitivity of TRAIL and/or IP-10 measured in pre-symptomatic healthcare workers (Index test) for PCR confirmed viral infections including COVID-19.

Secondary outcome

Secondary Objectives

1. To determine the diagnostic accuracy of TRAIL and/or IP-10 for detection of viral infections including COVID-19 during the early symptomatic phase in healthcare workers at increased risk for respiratory viral infection

2. To determine if TRAIL and/or IP-10 are related to severity of COVID-19 disease in healthcare workers after developing COVID-19

3. To identify additional candidate biomarkers to detect early viral infection

and/or disease severity in healthcare workers after developing COVID-19

4. To determine asymptomatic COVID-19 infections in healthcare workers

Secondary Endpoints

1. Sensitivity and specificity of TRAIL and/or IP-10 in early symptomatic

healthcare workersSensitivity and specificity of TRAIL and/or IP-10 in all

healthcare workers measured at maximum 48 hours before onset of symptoms

2. Sensitivity and specificity of TRAIL and/or IP-10 in all healthcare workers

measured every 24 hours

3. Sensitivity and specificity of TRAIL and/or IP-10 in pre-symptomatic

healthcare workers for PCR confirmed COVID-19 infection

4. Sensitivity and specificity of TRAIL and/or IP-10 in COVID-19 infected

healthcare workers related to disease severity mesasured on day 1, 2 and 3

after onset of symptoms

5. The proportion of healthcare workers with COVID-19 who are asymptomatic

Study description

Background summary

Why is it important to detect viral infection presymtomatically?

The novel coronavirus disease (COVID-19) is currently causing a pandemic affecting 197 countries up to now. To date, the World Health Organization (WHO) has reported 413,467 confirmed cases and 18,433 confirmed deaths. Controlling a viral outbreak like the current one requires early detection of the infection, before the infected individual passes on the virus. Ideally the detection should occur at the pre-symptomatic stage before symptom onset, when viral

titers may be undetectable but high enough to make an individual contagious. Earlier diagnosis of COVID-19 would be extremely relevant in the containment of the outbreak, as an infected person is already contagious before onset of symptoms as described for influenza. Pre-symptomatic spread of COVID-19 is currently topic of investigation.

If it would be possible to identify infected persons before showing symptoms, this may help to contain a future outbreak if COVID-19 re-enters our country in the future. It may even have more value if a unknown viral pathogen will emerge in the future that is very contagious before symptoms arise. Before pathogen specific PCR tests are developed and available on a large scale, a test that is able to detect any pre-symptomatic virus may make the difference between the ability to contain the virus or not before it spreads globally. So, a future outbreak could be prevented with rapid early detection when the causing agent is still unknown or rapid molecular viral diagnostics are still under development.

In addition, healthcare workers are at the front line in the battle against this outbreak, and it is at these crucial times when large percentages of hospital staff are potentially exposed, raising the question of whether they should go into quarantine. As the outbreak proceeds it becomes impractical to base isolation on potential exposure. Healthcare workers, unaware of their own infection, can inadvertently put their patients and co-workers at risk of infection, especially if the virus is contagious at a pre-symptomatic or early symptomatic stage. Identifying this individual as early as possible, isolating them from the environment and providing them with pre-emptive treatment if applicable, may be able to help to combat the outbreak.

In addition, managing an outbreak demands careful allocation of resources. Most antivirals are known to be most effective when applied in a very early stage in the disease, when the viral load is still low. If it would be possible to assess how likely a person is exhibit severe infection symptoms at this stage, it would help to make an informed decision on the expected risks and benefits of treatment in this individual and from a population perspective the need to allocate resources.

Study objective

In this study we aim to evaluate whether the levels of TRAIL and/or IP-10, alone or in combination, are a sign of viral infection at a stage before symptoms arise. We will assess the diagnostic value of the biomarkers alone and/or in combination, using various cutoffs, to evaluate the potential value in different situations in clinical practice and/or when new outbreaks arise.

Study design

We will perform a prospective cohort study. Healthcare workers without symptoms of respiratory tract infection (RTI), who have a high risk of infection due to exposure to viral RTI patients will be followed up for two to four weeks during the COVID-19 pandemic. Blood samples will be taken six times to measure the biomarkers TRAIL and IP-10 using ImmunoXpert (Index test), and within 2 days after symptoms occur the presence and type of viral infection will be determined by PCR using a respiratory sample (reference test).

Study burden and risks

This study is designed to examine the dynamics of the host response to COVID-19 infection. Patients participating in the study do not receive any investigational drug nor any experimental examination or procedure. The participants are exposed to the minimal risk associated with the collection of a venous blood sample (Phlebotomy) and with an additional, non-invasive nasal swab sampling.

The risk of standard phlebotomy may include infection, discomfort, pain or subcutaneous bleeding which may be caused by venous rupture. The risk in nasal swab sampling may include mainly discomfort or limited pain. The described procedures are very common in the clinical practice and are widely performed. In addition, the medical staff that will perform these procedures is highly qualified and experienced in performing these tests.

The participants in the study are not expected to have any direct benefit following their enrollment to the study. Study results will not affect the diagnosis, prognosis, or treatment of the participants. Still, by participating in the study, the subjects contribute to investigation of the host response to COVID-19 infection, with the goal of establishing host biomarker dynamics that are useful in managing the COVID-19 outbreak and future outbreaks.

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

Adult healthcare workers who have signed informed consent form will be eligible for inclusion. In order to be eligible to participate in this study, a subject must meet all of the following criteria:
* No symptoms of acute respiratory tract infection at time of enrollment
* No symptoms of acute respiratory tract infection in the previous two weeks
* Risk of exposure to COVID-19 infected patients defined by daily bedside care for patients

Exclusion criteria

A potential subject who meets the following criteria will be excluded from participation in this study:
* An incute respiratory infection during the previous two weeks
* Previously proven COVID-19 infection
* A proven or suspected HIV, HBV, or HCV infection
* Active malignancy
* Current treatment with immune-suppresives or immune-modulation therapies
* Severe illnesses that affect life expectancy and quality of life (other than suspected COVID-19 infection)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-04-2020
Enrollment:	333
Type:	Actual

Ethics review

Approved WMO Date:	06-04-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	29-04-2020
Application type:	Amendment
Review commission:	METC NedMec

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	NL73609.041.20