**Trial Description**

**Title**

Breath-assisted stimulation of the anti-inflammatory reflex of the vagus nerve in covid-19 disease: a randomized-controlled trial

**Trial Acronym**

BEAT-COVID (Breathing against COVID)

**URL of the trial**

[--]*

**Brief Summary in Lay Language**

**Aim of the study**

An important goal in combating the so-called corona pandemic is to ensure that as few people as possible become seriously ill. Not only the virus itself plays a role, but also the response of the own defense system (immune system) to the virus. It happens that the defense reaction is too strong, which makes the course of the disease more severe. An important starting point for preventing severe courses of the disease is therefore to prevent an excessive immune response. High-ranking research results show that there is an anti-inflammatory reflex in the body, which can be activated by a certain breathing technique with slowed exhalation. Whether this can also mitigate the inflammatory response in pre-existing viral diseases such as infection with the novel Corona virus has not yet been investigated.

The aim of this pilot study is to determine whether this breathing technique actually reduces inflammation levels in the blood of patients suffering from the novel corona virus. To do this, we will compare the levels of inflammation in the blood of patients who use this breathing technique with the levels of patients who do not use this breathing technique.

**Brief Summary in Scientific Language**

A major problem in the context of the pandemic with SARS-CoV-2 continues to be severe courses of disease that result not only directly from the virus-induced cellular damage but also from the sometimes vigorous immune response ("cytokine storm"). An intervention option that mitigates the immune response without compromising the defense against the virus is urgently needed.

The anti-inflammatory reflex mediated via the vagus nerve may provide such a pathway (Pavlov VA, Tracey KJ. Neural regulation of immunity: molecular mechanisms and clinical translation. Nat Neurosci 2017; 20: 156-166 & Leitzke M, Stefanovic D, Meyer J-J, et al. Autonomic balance determines the severity of COVID-19 courses. Bioelectron Med 2020; 6). This can be stimulated by a simple breathing technique. Whether this actually results in a clinically relevant change in inflammatory levels in the context of acute viral infection has not yet been investigated. The aim of our study is to investigate this question:

Can a breathing technique that increases vagotone decrease inflammatory levels in patients with SARS-CoV-2 infection compared to a control group of patients who also have SARS-CoV-2 infection but do not perform the breathing technique?
Do you plan to share individual participant data with other researchers?
Yes

Description IPD sharing plan
At the end of the primary evaluation, the data will be anonymized via the OPARU service of the University of Ulm and/or attached to the primary publication.

Organizational Data
- DRKS-ID: DRKS00023971
- Date of Registration in DRKS: 2021/02/02
- Date of Registration in Partner Registry or other Primary Registry: [---]*
- Investigator Sponsored/Initiated Trial (IST/IIT): yes
- Ethics Approval/Approval of the Ethics Committee: Approved
- (leading) Ethics Committee Nr.: 3/21, Ethik-Kommission der Universität Ulm

Secondary IDs
- Universal Trial Number (UTN): U1111-1263-8658

Health condition or Problem studied
- ICD10: U07.1 - Emergency use of U07.1
- Free text: Inpatients, hospitalized due to infection with SARS-CoV-2

Interventions/Observational Groups
- Arm 1: Intervention: Breathing exercise to stimulate vagal activity to stimulate the cholinergic anti-inflammatory reflex. Aim: 3x20min daily with 6 breaths per minute and an inhale to exhale ratio of 4:6.
- Arm 2: Control group: Treatment as Usual

Characteristics
- Study Type: Interventional
- Study Type Non-Interventional: [---]*
- Allocation: Randomized controlled trial
Study Type: **Interventional**

Allocation: **Randomized controlled trial**

- Blinding: [---]*
- Control: **Active control (effective treatment of control group)**
- Purpose: **Basic research/physiological study**
- Assignment: **Parallel**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

**Primary Outcome**

Course of inflammatory parameter IL-6 at admission (day 1) and bi-daily until discharge (average length of stay 10 days, i.e. 5 measurements on average)

**Secondary Outcome**

1.) Course of other inflammatory parameters leukocytes, CRP, TNF-alpha (Bi-daily)
2) subjective dyspnea on admission (day 1) and for two days until discharge (5 measurements), day 30 after discharge
3.) Onset of ventilator requirement and intensive care requirement within 30 days of first hospitalization and death by 30 days after discharge
4.) Length of stay in normal ward
5.) Course of SDNN (recorded on admission and then bi-daily)
6.) Outpatient course (query of Covid-19-associated symptoms such as fatigue 30 days after discharge)

**Countries of recruitment**

- DE Germany

**Locations of Recruitment**

- University Medical Center **Klinik für Innere Medizin I, Ulm**
- University Medical Center **Klinik für Innere Medizin III, Ulm**

**Recruitment**

-
Planned/Actual: **Planned**

- (Anticipated or Actual) Date of First Enrollment: **2021/02/21**
- Target Sample Size: **60**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

**Inclusion Criteria**

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

**Additional Inclusion Criteria**

- SARS-CoV-2-infected patients hospitalized in "normal wards" (Not ICU) with a maximum moderate degree of disease according to RKI/WHO definition (see first exclusion criterion)
- Age min. 18 years
- Able to give informed consent at the time of study inclusion

**Exclusion criteria**

- severe covid pneumonia with fever and bilateral lung infiltrates and respiratory rate>30/min or SpO2<90% on room air (adapted from RKI/WHO)
- Condition after surgery/trauma/acute event (stroke, myocardial infarction, acute covid-independent infection) in the last 4 weeks
- Known pregnancy
- Patients with pre-existing pulmonary disease who were on oxygen prior to infection (e.g., due to pulmonary fibrosis, COPD)
- limited ability to give consent (e.g. due to dementia)
- limited ability to perform breathing maneuvers independently (e.g. high frailty)
- limited ability to provide self-care (care level 2 or 3)
- lack of language skills
- seizures in the medical history

**Addresses**

- **Primary Sponsor**
  
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Sources of Monetary or Material Support

- Institutional budget, no external funding (budget of sponsor/PI)

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Status

- Recruitment Status: Recruiting ongoing
- Study Closing (LPLV): [---]*

Trial Publications, Results and other documents

* This entry means the parameter is not applicable or has not been set.
*** This entry means that data is not displayed due to insufficient data privacy clearing.