Garching near Munich, June 2020

Press Release:

Cold plasma could increase the chances of survival for mechanically ventilated COVID-19 patients.

Cold atmospheric plasma (CAP) treatment inactivates bacteria and viruses. If CAP were used in the nasal, oral, and pharyngeal cavities, nosocomial superinfections in patients with mechanical ventilators, which are a frequent cause of death, could potentially be avoided.

In recent weeks, the promising use of cold plasma for treating COVID-19 patients has been discussed with virologists, microbiologists, anaesthesiologists, intensive care physicians, and pulmonologists. It is known that cold plasmas have a very broad spectrum of efficacy against bacteria – including multi-drug resistant organisms such as MRSA – and viruses. The latter has been demonstrated on adenoviruses and noroviruses, among others. Thus, the supposition that coronaviruses may also be inactivated by cold plasma seemed obvious. As a result of a collaboration with the von Brunn research group at the Max-von-Pettenkofer Institute in Munich, there are first indications that cold atmospheric plasma can also inactivate coronaviruses in solution. With these promising results, the development of the so-called 'plasma intensive care' started at terraplasma medical GmbH – a device for generating gaseous cold plasma, which, in contrast to antiseptic liquids, can also reach angled or hard-to-reach areas in the upper respiratory tract. Overarching aim is to use the plasma intensive care on mechanically ventilated COVID-19 patients in order to reduce the viral load and to prevent bacterial pneumonia.

The basis for this development is provided by the plasma care®, a CE-mark approved medical device that generates cold atmospheric plasma. It was developed for the mobile treatment of acute and chronic wounds. The plasma intensive care is an adaptation of the plasma care® for anti-bacterial and anti-viral treatment of the upper respiratory tract, and is thus intended to improve the oral hygiene of patients with mechanical ventilators in general, and specifically that of COVID-19 patients. The plasma intensive care allows gaseous cold plasma to flow into the nasal, oral and pharyngeal cavities and temporarily floods them. Application of cold plasma is expected to inactivate bacteria and viruses locally to prevent them from penetrating bronchi and lungs. This could reduce the risk of nosocomial pneumonia and increase the chances of survival for these patients.

Cold plasma inactivates bacteria and viruses by means of several physical and chemical processes. Even in the case of existing antibiotic resistance(s), the effectiveness against bacteria is not impaired. *In vitro* studies have shown that cold atmospheric plasma achieves a bacterial reduction of up to 99.999 percent on agar within an application time of only 3 minutes. Furthermore, it has been demonstrated that various human pathogenic viruses are sensitive towards cold plasma.

The long-term goal when using cold atmospheric plasma in the nasal, oral, and pharyngeal cavities is to avoid mechanical ventilation by means of preventive treatment of viral infections of the upper respiratory tract. If an early-stage treatment significantly reduces the viral load, it may be possible to avoid the penetration of the virus into the lower respiratory tract. However, as cold plasma can reach the lungs of patients who breathe independently the potential effects resulting therefrom are currently investigated. Research projects are being initiated together with the Fraunhofer Institute for Toxicology and Experimental Medicine and the university hospitals in Regensburg and Munich. terraplasma medical GmbH expects to have the first results in about 6 – 7 months.

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Background information:

The situation and treatment of COVID-19 patients with mechanical ventilators.

SARS-CoV-2 displays high replication activity in the upper respiratory tract in the early stages of the disease [1]. Vaccinations for the prevention, or medication for the treatment of the respiratory disease COVID-19, triggered by SARS-CoV-2, are not available yet. In the case of a severe course of the disease, COVID-19 patients often require mechanical ventilators due to severe hypoxia and possible lung failure, which is a severe intervention fraught with risks. In particular the risk of acquiring nosocomial superinfections of the lung increases sharply. In individual studies, half of the patients with mechanical ventilators who did not survive were found to have a bacterial superinfection [2]. Previous virus pandemics (e.g. SARS, MERS, H1N1) have shown that 30% to 55% of deaths were caused by secondary bacterial pneumonia [3].

What is cold plasma and how does it work?

Cold plasma is a partially ionised gas. It creates a reactive mix of electrons, ions, excited atoms and molecules, reactive chemical species (such as O3, NO, NO2, etc.), UV radiation and heat. It penetrates the bacterial cell wall and membrane and destroys the intracellular structures of these microorganisms, including the DNA, so that they are inactivated. The mechanism of virus inactivation by means of cold atmospheric plasma is not yet fully

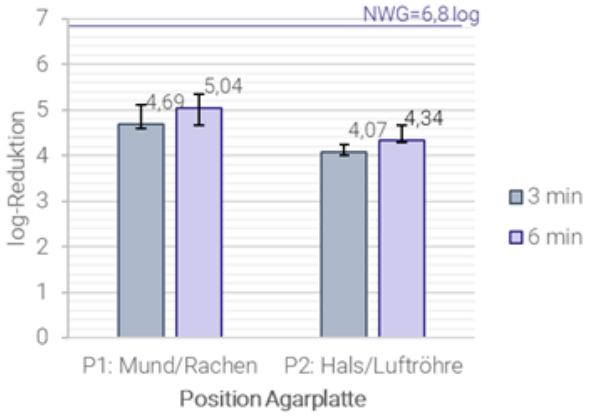
understood. Several studies suggest that reactive nitrogen species can lead to the denaturation of viral proteins. Human eukaryotic cells are generally better protected, because the DNA is located within the cell nucleus and because of cellular survival mechanisms.

In vitro test results:

The plasma care® has been pre-clinically tested on different microorganisms, with very promising results:

99.999% of bacteria, including multi-drug resistant organisms such as MRSA or VRE, are inactivated on agar within a treatment time of 1 minute. Viruses (adenoviruses in solution) can be inactivated by up to 99.999% after a 4-minute treatment. Coronaviruses in solution can also be inactivated; the effectiveness and the required treatment time are currently being investigated.

The plasma care® has already been used successfully in clinical practice for the treatment of infected wounds.



In order to be able to provide a statement about the antimicrobial effect of the plasma intensive care, the developers have created a model that simulates the nasal, oral, and pharyngeal cavities down to the subglottal cavity (measuring points: nose, mouth, pharynx, subglottis). This model was used to investigate the effectiveness of gaseous cold plasma against bacteria. The results are very encouraging as the tests showed a bacterial log-reduction on agar of about 4.5 – 5 log (approx. 99.999%) at the "pharynx" measuring point and of about 4 – 4.5 log (approx. 99.99%) at the "subglottis" measuring point after only 3 minutes of treatment.

Sources:

[1] C.H.M. Drosten, Warum COVID-19 ansteckender ist als Sars ("Why COVID-19 is more contagious than Sars"), Tagesspiegel, February 2020
[2] F. Zhou, et. al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study, The Lancet, March 2020
[3] J.L. Gerberding, Antibiotic resistance: the hidden threat lurking behind COVID-19, STAT, March 2020

Company profile:

terraplasma medical GmbH combines the research expertise of the terraplasma GmbH with the medical technology know-how of the Dynamify GmbH/today, DITABIS AG.

terraplasma GmbH researches cold atmospheric plasmas (for short: CAPs). CAPs are partially ionised gases that very efficiently inactivate bacteria, fungi, viruses, spores or even odour molecules.

Dynamify GmbH – today DITABIS AG – is an OEM developer and manufacturer of medical devices which covers the holistic product life cycle of a medical device. This includes development, approval processes, production as well as maintenance and servicing.

The two companies founded terraplasma medical GmbH with the aim of developing the plasma care®. The idea: transformation of the highly complex plasma technology into a small, convenient and affordable medical device, used primarily for wound treatment in outpatient care.

Background information: 576 words

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