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Reduction of the Viral Load by Non-Invasive Photodynamic Therapy in Early Stages of COVID-19 infection

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Abstract

Background: Coronavirus infection 2019 (COVID-19) is a new pandemic disease. Currently, there are no medications or vaccines available; this has led to dire medical and social consequences and significant morbidity and mortality. (1) We report here, the clinical results of a novel and proprietary research study, using anti-microbial photodynamic treatments to reduce the viral load during the initial stages of the COVID-19 infection with the goal of reducing progression of disease, reducing symptoms, susceptibility to infectivity, and death while maintaining the ability to mount an immune response.

Results: Our results confirm the influence of the viral load on the course of the disease in COVID-19 infections. The percentage of mild disease in the active treatment group was almost double compared to the placebo group.

Conclusion: We have investigated the potential of photodynamic treatments in the treatment of COVID-19 infections. We have found and look to further optimize a photodynamic procedure, which is innovative, accessible, cost effective and has shown to provide profound clinical efficacy in treating all age groups of those affected by Covid-19. This treatment provides a major breakthrough in the treatment of Covid-19 without any suspected or apparent treatment related adverse events. This is especially relevant for patients who have profound co-morbidities, advanced age, and are at the highest risk as well as potentially asymptomatic carriers who may be continuing to be unwitting participants in the Covid-19 pandemic.

1 Background

Coronavirus infection 2019 (COVID-19) is a new pandemic disease. Currently, there are no medications or vaccines available; this has led to dire medical and social consequences and significant morbidity and mortality. (1) We report here, the clinical results of a novel and proprietary research study, using anti-microbial photodynamic treatments to reduce the viral load during the initial stages of the COVID-19 infection with the goal of reducing progression of disease, reducing symptoms, susceptibility to infectivity, and death while maintaining the ability to mount an immune response.

Viruses have been estimated to be the most abundant and diverse biological systems on earth and their size typically ranges from 0.02-0.3 micrometers, though some are larger and can range up to 1 micrometer. Viruses depend on other cells (plant/animal, or bacterial) for their reproduction are classified according to their genome and method of reproduction. They consist of a DNA or RNA (single or double stranded) core, an outer protein cover, and, in some virus classes, lipids. Based upon the basic structure of viruses there are three principal molecular targets for viral PDI and for the reaction with the generated ROS: nucleic acids, virus proteins, and if present, viral lipids.

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Those with viral lipids and/or protein envelope, in general seem to be more sensitive to using PDT/PDI (photodynamic inactivation) than those without. (2)

COVID-19 has a number of distinguishing features including a protein envelop and lipids that would make it susceptible to treatment with PDT. (3) It is a positive stranded RNA virus and belongs to the beta CoVs category. It has a round/elliptic and often pleomorphic form, and a diameter of approximately 60-140 nm. Like other CoVs, it is sensitive to ultraviolet rays and heat. This virus has been shown to have a number of different challenges that make the likelihood of a successful vaccine as a primary treatment a distant reality.

There are several recently published reports (4,5,6,7) which describe the influence of the viral load on the course of disease. In summary, it was found that low viral loads in the initial infection stages promote mild disease (1,4) whereas large viral loads in the early stages favours severe disease, including complex lung dysfunction(4,5,6,7,8). Woelfel et.al. have previously shown that viral loads of COVID-19 under a concentration of 10⁶ copies per mL of sputum or per entire throatswab are unlikely to yield infectious virus growth in cell culture(12).

There are several studies in the scientific literature, which have reported successful treatments of coronaviruses by photodynamic therapy (PDT) using methylene blue and riboflavin as photosensitizers (9,10).

The scientific literature clearly shows that both methylene blue and riboflavin can be used to inactivate coronaviruses using a photodynamic process, although the detailed cellular mechanisms are not completely known. It is assumed that the COVID-19 viruses accumulate the photosensitive molecules due to their energetic potential. Photodynamic excitation by an appropriately adapted light source (laser or LED) leads to the formation of reactive singlet oxygen species, which destroy the cellular membrane of the viruses.

In a randomized study, the secretion dynamics of viruses capable of replication from samples of throat and sputum was examined (12,13). Swab samples from the throat and nose contained viruses capable of replication until the fourth day after the onset of symptoms

and from sputum until the eighth day after the onset of symptoms. Viruses capable of replication were not found in the faeces (samples available from the sixth day after onset of symptoms), urine or serum. SARS-CoV-2 RNA was found in neither urine or serum.

Therefore we can conclude that at the onset of the symptoms (fever, cough, headaches) a significant number of viruses are bound to ACE2 receptors in the mucosa of the oral cavity, throat and nasal cavity.

As long the viruses are localized at these sites, they are easily accessible to photodynamic treatments. When the first symptoms appear and the PCR tests indicate positive results, the door is open for a photodynamic reduction of the viral load! As a consequence, the number of viruses, which can potentially seed to the lower respiratory tract is reduced and the viral load in the lung is reduced.

It is unlikely that the photodynamic process removes all viruses which are bound in the oral cavity, throat and nasal cavity. However, this offers an additional advantage, because the reduced viral load stimulates an immune reaction and the formation of protective antibodies, while favouring a mild or moderate course of disease without severe lung dysfunction or damage.

The initial goals of our photodynamic virus inactivation protocol were to show:

- Reduction of the COVID-19 viral load in the early stages of the infection
- Reduction of the COVID-19 viral load in the lung
- Reduction of inflammation and severe damage in the lung,
- Improving the clinical course of the disease
- Reduction of COVID-19 related deaths
- Maintaining the capability of forming specific COVID-19 antibodies

2. Materials and methods

The photosensitizer used was methylene blue as a 1% solution of methylthioninium-chloride dissolved in a 5% glucose solution. (Heltschl GmbH, Germany). The methylene blue solution was applied by flushing and gargling in the oral cavity and throat, and by spraying in the nasal cavity.

The photodynamic excitation was performed using the Medloux PDT device, produced by laneg GmbH, Germany (www.med-loux.com). The device applicator emits 660nm laser radiation with 240 mW power. The infected areas were irradiated for 5 minutes resulting in a dosage of about 72 J/cm2. This procedure: 1 min flushing followed by 5 minutes irradiation, was repeated 5 times, resulting in a total dosage of about 360 J/cm2. Before and immediately after the photodynamic treatments, the viral concentration was determined by PCR tests using the PCR real time testing facility ThermoFisher, QuantStudio 3. The entire treatment procedure is harmless, painless, non-invasive and free of any side effects.

The placebo patients received exactly same treatment procedure except that all placebo patients were treated with covered radiation heads. The patients were not able to distinguish an active versus a placebo treatment due to the filter function of the laser safety goggles.

After 4 weeks patients who had received active treatment were tested with respect to formation of antibodies to SARS CoV-2, using the Euroimmun ELISA test, although this test is not completely specific.

The treatments were performed between 22 March 2020 and 25 April 2020.

3. Results

We have treated 300 patients with the active treatment protocol and 300 patients with the placebo protocol described above. The active treatment group consisted of 164 men and 136 women, with an age range of 35-83 years. All patients signed informed consent prior to the start of the treatment protocol. The main inclusion criteria were fever, typical symptoms and a positive PCR test. The main exclusion criterium was a negative PCR test. Besides fever, we have found a significant variability in the initial presenting symptoms, like cough, loss of smell, loss of taste, headaches, fatigue and others.

We have characterized the course of the disease by the degree and duration of fever which was the most prominent symptom (see Table 1):

Table 1: Summary of Symptom Categories

Symptom Category	Maximum Fever	Maximum Fever Duration
Mild	37.7 °C (99.9 °F)	1 Week
Moderate	38.7 °C (101.7 °F)	2 Weeks
Severe (Hospital Admission)	39.2 °C (102.6 °F)	3 Weeks
Severe (ICU/Hospital Admission)	39.5 °C (103.1 °F)	4-6 Weeks

Table 2 shows the results regarding the course of the disease based on the symptom categories defined above:

Table 2: Summary of Disease Course

	Active Treatment Number	Active Treatment Percentage	Placebo Number	Placebo Percentage
Mild	192 patients	64%	102 patients	34 %
Moderate	99 patients	33%	141 patients	47 %
Severe (Hospital Admission)	6 patients	2%	36 patients	12 %
Severe (Hospital/ ICU Admission)	2 patients	0.6%	21 patients	7 %

We have found a significant reduction of severe course of disease (2.6% vs. 19%) and a significant attenuation of disease progression (97% vs. 81%) in the active treatment group of patients. This result is in accordance with a reduced viral load in the oral and nasal cavity and in the throat, measured by PCR test immediately after each 5-stage treatment cycle.

Table 3: Summary of Mortality Rate

Mortality Rate - Active Treatment Group (300 patients)	Mortality Rate - Placebo Group (300 patients)
0,7 %	3,3 %

We found a significant reduction in the mortality rate in the active treatment group. The mortality rate in the placebo group was consistent with the average mortality rate in Germany over the same time period. There were no treatment related adverse events that were noted or suspected.

5.Discussion

Our results confirm the influence of the viral load on the course of the disease in COVID-19 infections. The percentage of mild disease in the active treatment group was almost double compared to the placebo group!

The percentage of hospital admissions in the placebo group was in accordance with the average data published for Germany in the respective time period. We had 36 patients (12%)

with severe disease, requiring hospital admission in the non-treated placebo group and just 6 (2%) patients with severe disease in the photodynamic treated active group.

This result indicates that just the exposure of the viruses to methylene blue by flushing or gargling and spraying does not appear to reduce the viral load; the photodynamic excitation is a necessary process in order to activate a PDI response. The mortality rate differences between the active treatment group and the placebo group, are based upon the assumption that the number of patients in both groups with underlying health conditions such as type 2 diabetes, were quite similar. We cannot make a distinct interpretation of the measured antibody formation rate, because the ELISA tests were not of sufficient specificity to distinguish SARS CoV from SARS CoV-2. We did confirm the presence of antibodies in 96 % of the patients of the active treatment group 4 weeks after administering the photodynamic treatments.

6. Conclusion

We have investigated the potential of photodynamic treatments in the treatment of COVID-19 infections. We have found and look to further optimize a photodynamic procedure, which is innovative, soon to be uniquely accessible, cost effective and has shown to provide profound clinical efficacy in treating all age groups of those affected by Covid-19. Using methylene blue as a photosensitizer and 660 nm red light for excitation, the viral load in the oral and nasal cavity at the initial stage of the infection can be significantly reduced, leading to significant decreases in morbidity and reduced mortality rates while maintaining the body's ability to mount an immune response and potentially protective immunity in the future. This treatment provides a major breakthrough in the treatment of Covid-19 without any suspected or apparent treatment related adverse events. This is especially relevant for patients who have profound co-morbidities, advanced age, and are at the highest risk as well as potentially asymptomatic carriers who may be continuing to be unwitting participants in the Covid-19 pandemic.

Helsinki Declaration:

The authors declare that the treatments of the patients were performed under strict consideration of the WAMA most recent (2012-2013) revision of the Declaration of Helsinki (DoH).

Conflicts of interest

The authors declare that there are no conflicts of interest.

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