PROSPECTIVE, PARALLEL, MULTI-CENTER, RANDOMIZED CONTROLLED STUDY OF THE EFFECTS OF TURKISH BEAM-UVC BEAM AND LASER BEAM TREATMENT ACCORDING TO STANDARD TREATMENT.

STUDY PROTOCOL
"CONFIDENTIAL"

Coordinator Researcher: Prof. Dr. Hikmet Selçuk GEDIK

Clinical Trial Centers: Ankara University Medical Faculty , *Infectious Diseases and Clinical Microbiology*

Gazi University Medical Faculty ,Cardiovascular Surgery

Sağlik Bilimleri University-GATA, *Infectious Diseases and Clinical Microbiology*

Sağlik Bilimleri University Ankara Sehir Hospital, Enfeksiyon Hastaliklari ve Klinik Mikrobiyoloji ABD

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Afyon Kocatepe University Medical Faculty Hospital, Pediatrics-Neonatology

Gaziantep University Medical Faculty Emergency Medicine and Internal Diseases Intensive Care Unit

Project Management: ***RD GLOBAL ARASTIRMA GELISTIRME SAĞLIK ILAÇ INSAAT YATIRIMLARI A.S.***

Contracted Consultant Organization: Gazi University,Ankara

Gaziantep University Farmagen IKU Merkezi, Gaziantep

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1.0 SUMMARY of INVESTIGATION

Study Title: Prospective, Parallel, Multicenter Randomized Controlled Study Investigating the Effects of UVC Beam and Laser Beam Therapy According to Standard Therapy in Patients with Covid-19 Diagnosis

Study Code: MD2020/001

Device : Turkishbeam Model Number: 1007-001

**: The device was produced by RD GLOBAL ARASTIRMA GELISTIRME SAĞLIK ILAÇ INSAAT YATIRIMLARI A.S.*

Device Classification: Class III

Purpose of the Study: Clinical research study that evaluates the effect of Turkish Beam-Selective UV developed by RD GLOBAL ARASTIRMA GELISTIRME SAĞLIK ILAÇ INSAAT YATIRIMLARI A.S. use into Intravascular, Intrapulmonary, Intratracial, Intrarespiratory area. Bacteria, Fungal and Virus-based pathogens systematically to collect and evaluate specific clinical performance and safety data.

In our Clinical Research, we aimed to investigate the effectiveness of the treatment group and control group mortality rates, intensive care hospitalization times, monitoring the virus load by PCR, and the treatment effectiveness of UVC application.

Scope of the Study: This Clinical Research covers determining the treatment effectiveness and reliability of UVC application to patient groups, the details of which are determined in the protocol.

Application: Intravascular, Intrapulmonary, Intratracial, Intrarespiratory UVC and Laser Therapy System

Overall Study Design: Prospective, Parellel, Multicenter, Randomized Controlled

Number of volunteers: 50 patient- 2 groups with 25 (two hundred) patients in each group

Treatment Groups: Test: *Antiviral + Antimalarial + Antibiotic Treatment + UVC Therapy*
Control: *Antiviral + Antimalarial + Antibiotic Treatment*

Groups of Volunteer: Those who are between the ages of 40-75 and who have applied to the clinic with symptoms such as fever, weakness, cough, and shortness of breath, or who have signs of COVID-19 (SARS-CoV-2) test positive or atypical pneumonia findings in CT findings and accepted as COVID 19 infection, and patients undergoing intubation treatment in intensive care unit

Sensitive population / Vulnerable subjects: The study will not include under-40, pregnant women and those with suspected pregnancy, previously diagnosed with mental disorders, puerperant women and lactating women..

Duration of the clinical trial: 3 months (04.2020- 07.2020)

Researched Medical Condition: and Disease

According to ICD 10 coding;
B34.9 Virus infection is not defined,
B34.2 CORONA VIRUS INFECTION UNDEFINED
B97.2 Colon virus, causative agent of diseases classified in other sections
B97 Viral agents, the cause of diseases classified in other sections
B99 infectious diseases, other and unspecified
A49.9 bacterial infection not defined

Manufacturer of the Device:

RD Global Arastirma Gelistirme Sağlik Ilaç Insaat Yatirimlari A.S.

Ethics Committees:	Gaziantep University, Klinik Arastirmalar Etik Kurulu
IKU Statement:	This study will be conducted in accordance with the principles of Good Clinical Practice (IKU), the Declaration of Helsinki and the requirements of the legal documents published on this subject.
Privacy:	The name of the Clinical Research Coordinator, Responsible Researcher and Assistant Researcher will be included in the reports. The names of the patients will be kept Confidential. Patient datas will be used by assigning CODE to each patient. Data privacy will be ensured under the "KVKK" *(PDPL-Personal Data Protection Law)*. Identification information / personal identifier of the volunteers such as Patient card, Patient diary will be collected or accessed. It will be ensured that the relevant person to be researched has a written consent based on adequate information about the nature and results of the research and that this consent is not dependent on any benefits. Responsible / assistant researchers will receive relevant written commitment on ethics, confidentiality and "PDPL" on this issue.

1.1 PRINCIPLE INVESTIGATORS

Coordinator: Prof. Dr. Hikmet Selçuk GEDIK
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Clinical Trial Centers		
	Name of Center	**Principle Investigator (Proffession) (Telephone)**
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1	*Gazi University Medical Faculty KVC Anabilim Dali*	*Assoc. Prof. Mustafa Hakan ZOR (Cardiovascular Surgery Specialist) (0505 299 7777)*
2	*Sağlik Bilimleri University-GATA*	*Prof. Kemalettin AYDIN (Infectious Diseases and Clinical Microbiology) (0532 424 9848)*
3	*Sağlik Bilimleri University Ankara Sehir Hospital*	*Prof. Rahmet GUNER (Infectious Diseases and Clinical Microbiology)*
4	*Yeditepe University Hospital*	*Assoc. Prof. Halit YEREBAKAN (Cardiovascular Surgery Specialist) (0533 271 9284)*
5	*Istanbul Bakirkoy Sadi Konuk Eğitim ve Arastirma Hospital Cardiovascular Surgery*	*Prof. Ahmet AKGUL (Cardiovascular Surgery Specialist) (05322547203)*
6	Suleyman Demirel University Medical Faculty Hospital,	*Prof. Turhan YAVUZ (Cardiovascular Surgery Specialist) (0546 730 4090)*
7	Afyon Kocatepe University Medical Faculty Hospital	*Prof. Nurullah OKUMUS (Pediatrics-Neonatology - RECTOR)*
8	*Gaziantep University Medical Faculty Emergency Medicine ve Iç Hastaliklari ABD Yogun Bakim Unitesi*	*Prof. Sevki Hakan EREN (Emergency Medicine) Dr.. Gulseren ELAY(Internal Intensive Care)*

CO-INVESTIGATORS

Name of Center	*Gazi University Medical Faculty*		
Address	*Cardiovascular Surgery*		
Position	**Name Surname**	**Title**	**Branch**
Co-Investigator	*Ozlem Güzel Tunçcan*	*Prof.*	*Infectious Diseases and Clinical Microbiology*
Co-Investigator	*Ozlem Gülbahar*	*Prof.*	*Medical Biochemistry*
Co-Investigator	*Dilek Erer*	*Prof.*	*Cardiac Surgery*
Co-Investigator	*Gulendam BOZDAYI*	*Prof.*	*Medical Microbiology*
Co-Investigator	*Pinar UYAR GOÇUN*	*Doç.*	*Medical Pathology*
Name of Center	*Sağlik Bilimleri University-GATA*		
Address	*Infectious Diseases and Clinical Microbiology*		
Position	**Name Surname**	**Title**	**Branch**
Co-Investigator	*Umit Savasçi*	*Associate Professor*	*Infectious Diseases and Clinical Microbiology*

Independent Data Monitoring Committee (Data Monitoring Group or Data Security Monitoring Committee)

Position	**Name Surname**	**Title**	**Branch**
Committee member	Orhan KOÇ	Op. Dr.	Pediatric Surgery Specialist
Committee member	Ufuk DEMIRKILIÇ	Prof.	Cardiovascular Surgery Specialist
Committee member	Evren EKINGEN	Specialst	Emergency Medicine Specialist

2.0 DESIGN of STUDY

2.1 DESIGN

Prospective, parallel, multicentre, randomized controlled study Ages between 40 and 75 years of age and positive symptoms such as fever, malaise, cough, and shortness of breath, or positive atypical pneumonia in CT findings or COVID-19 (SARS-CoV-2) test In the intensive care unit, which is accepted as COVID 19 infection and has been treated, patients will be treated with UVC radiation and laser beam treatment according to IKU principles in addition to Antimalarial therapy + Antiviral therapy + Anitibiotic therapy. Standard

treatment consisting of Antimalarial therapy + Antiviral therapy + Antibiotic therapy will be applied to the control group. The dosage of the standard treatment consisting of antimalarial therapy + Antiviral therapy + Anitibiotic therapy, the number of days of treatment, and its active ingredient are indicated in the table.

Treatment in Possible / Definitive COVID 19 Cases with Pneumonia		
Oseltamivir** tb 75 mg Hydroxychloroquine, 200 mg tablet	2x75 mg, oral Following 2x400 mg loading dose, 2x200 mg tablet orally	5 days 5 days
According to the physician's decision		
+$ Azithromycin ***	Day 1 500 mg, oral 4 days following 250 mg/day	5 days
Severe cases that did not respond to the first treatment		
Favipravir 200 mg tablet Or Lopinavir 200 mg / ritonavir 50mg tablet	2 x 1600 mg 2 x 600 mg 2 x 2 tablet, oral	5-7 days 10-14 days

Source: COVID-19 (SARS-CoV2 INFECTION) GUIDE (Scientific Board Study)
T. C. MINISTRY OF HEALTH 25 MARCH 2020

3.0 AIM of THE STUDY

With the application of ultraviolet light, it is aimed to treat the patient by seriously reducing / eliminating the burden of microorganism and inflammation in the patient body. The proposed treatment is an antimicrobial treatment strategy, and it is recommended to combine the supportive treatments with this process in terms of a holistic treatment strategy according to the clinical course of the disease.

4.0 INFORMATION ABOUT STUDY

Mechanism of Action

Ultraviolet (UV) irradiation is electromagnetic irradiation with a wavelength (100-400 nm) shorter than visible light (400-700 nm) but longer than x-rays (<100 nm). UV irradiation is divided into four separate spectral areas, including vacuum UV (100-200 nm), UVC (200-280 nm), UVB (280-315 nm) and UVA (315-400 nm). The mechanism of UVC inactivation of microorganisms is to damage the genetic material in the nucleus of the cell or nucleic acids in the virus. The UVC spectrum, especially the 250-270 nm range, is strongly absorbed by the nucleic acids of a microorganism and is therefore the inactivation wavelength range for microorganisms. This range, with a peak antimicrobial wavelength of

254nm, is known as the antimicrobial spectrum. Light-induced damage to the DNA or RNA of a microorganism usually results from dimerization of pyrimidine molecules. In particular, thymine (found only in DNA) produces cyclobutane dimers. When thymine molecules are dimerized, it becomes very difficult for nucleic acids to multiply, and if replication occurs, it often produces damage that prevents the viability of the microorganism. [1].

4.1 Usage Areas of UV

- Air Sterilization
- Surface Sterilization
- Water Sterilization, Water Treatment systems
- Instrument and Equipment Disinfection
- Disinfection of Food Packaging
- Use of tuberculosis patients in the ventilation system.
- It has many applications including the use of UVC in odor control, wastewater facilities, farms, commercial kitchens (HVAC) and food processing facilities.
- UVC germicidal lamps are also critical for purifying the air in industries where harmful and toxic chemicals such as printing, plastic and rubber are produced.
- In the disinfection of the air and surfaces of the operating rooms, Clean Room laboratories and biological safety cabinets, and inhibition of microorganisms in the air in the production area with UV-C light applications.
- Blood products have the potential to significantly reduce hepatitis C virus (HCV) infections.
- It is frequently used in sterilization of blood and plasma products.

4.2 Properties of UV

4.2.1 UV Properties UV 254 nm UV-C ray:

- It is a well-known and essential antimicrobial agent.
- Produces non-lethal pathogen damage to stop proliferation and increases sensitivity to immune system disruption.

450 nm Blue Laser beam:

- It regulates our biological rhythms.
- It regulates hormone balance.
- My vitamins increase absorption.
- It regulates the release of serotonin and cortisol.

535 nm Green Laser beam:

- To improve the behavior and functions of red blood cells,
- Increases the flexibility of red blood cells and provides more oxygen to the tissues.
- Improves hemodynamics with decreased blood viscosity.
- It has the feature of enabling restorative and balancing ways.

630 nm Red Laser beam:

- Increases cellular energy level.
- It reduces the production of proinflammatory cytokines.
- Immune regulates cell functions, slows or stops infection.

The effects of LED phototherapy depend on wavelength, power density, bacterial amount (or number), and species. Growth of S. aureus, E. coli and P. gingivalis increased at 625 nm, while 425 and 525nm showed bactericidal effect. In particular, S. aureus is inactivated only by applying 525 nm. [9].

The bactericidal effects of 625, 525 and 425 nm wavelength LED irradiation were investigated in vitro for anaerobic bacteria Porphyromonas gingivalis and two aerobes (Staphylococcus aureus and Escherichia coli DH5a). [9]. It shows that 625nm irradiation has potential applications for oral periodontal disease. This can be expected to have additional benefits for tooth whitening and resin curing in dental clinical practice. Irradiation at 625 nm can reduce inflammatory reactions and induce cell proliferation in periodontal disease involving the interaction of bacteria and oral cells. However, we can conclude that 625 nm irradiation has potential applications for periodontal. [9].

Blue light with wavelengths ranging from 400 to 470 nm has been reported to be effective for inhibiting various bacteria and fungi. Both experimental data and model simulation results have shown that 415-nm light has a more effective antifungal result that deals less damage to epithelial cells than 405-nm and 450-nm light. [3].

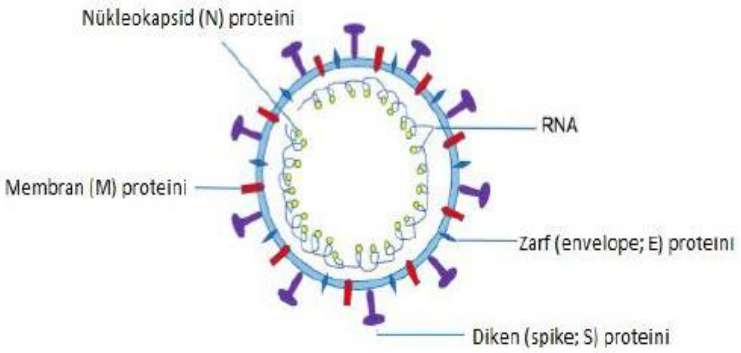
4.3 Precautions

- In the use of the product only, it should be performed by physicians who are cardiovascular surgeons, chest diseases, thoracic surgeries, intensive care specialists who will intervene with the patient with the tractors who have been trained in the product. In addition, the relevant branches (cardiovascular surgery, thoracic diseases, thoracic surgery, intensive care specialist) who will use the product in the clinical field, responsible researchers and assistant researchers will be planned and delivered about the device.
- Inspect product packaging prior to use.
- Do not use if sterile barrier is opened or damaged.
- Use prior to expiration date.
- Before starting the procedure, using protective glasses with UV filter feature for the patient, using eye bands for the patient to completely close the eyes when they do not have glasses.
- Use of UV filter protective glasses for the physician or healthcare personnel to use the device.
- Before using this product, principles, clinical practices, and associated risks must be fully learned.
- Each set used in treatment is for single use. It should not be used in the treatment of patients other than infection risk. SHOULD NOT BE STERILIZED AGAIN.
- If need to use The Disposable Steerable Catheter (disposable CAMERA CATHETER) and the fiberoptic line should be checked for operation before use; make sure that the size and shape of the catheter is suitable for the procedure to be performed
- Do not resterilize, as device performance may be compromised and there is an increased risk of cross contamination due to improper rework.

- If you encounter difficulties during the process, identify the cause of the strain before continuing
- Do not expose the product to autoclave or organic solvents.
- Pay attention to the expiration date stated on the package.
- Do not use the product that has exceeded the origin.
- Check the package and the material before use.
- Do not use the product that shows any problem.
- Use an appropriately sized guiding catheter or a guiding sheath.
- If you have difficulty during the procedure, identify the cause of the strain before continuing.

4.5 General Information About Coronavirus

Coronaviruses are single-chain, positive-polar, enveloped RNA viruses. Because they have positive polarity, they do not contain RNA-dependent RNA polymerase enzymes, but in their genomes they encode this enzyme. They have rodlike extensions on their surfaces. These viruses are named as Coronavirus (Figures 1 and 2) based on the meaning of "corona", that is "crown" in Latin (Figures 1 and 2).



Şekil 1. *Coronavirus*'un şematik yapısı (*Zhou Y, Yang Y, Huang J, Jiang S, Du L. Advances in MERS-CoV Vaccines and Therapeutics Based on the Receptor-Binding Domain. Viruses. 2019 Jan 14;11(1)).*

Figure 1 . Schematic Structure Of Covid-19 (Zhou Y, Yang Y, Huang J, Jiang S, Du L. Advances in MERS-CoV Vaccines and Therapeutics Based on the Receptor- Binding Domain. Viruses. 2019 Jan 14;11(1)).

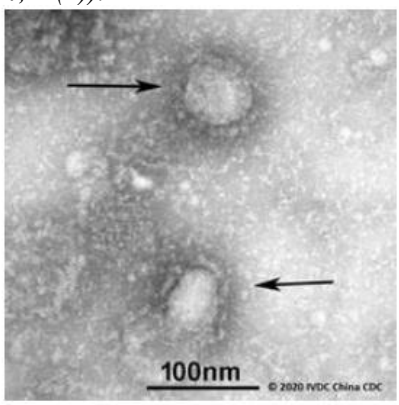
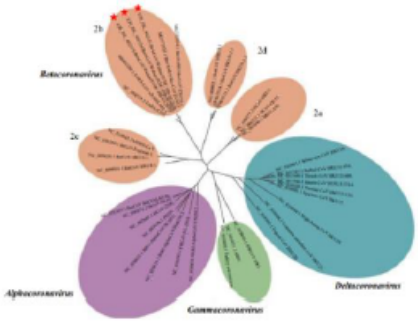


Figure 2: New Coronavirus (betacoronavirus) electron microscope image (https://www.gisaid.org/,son access date: 20.01.2020)

Coronaviruses are in the Coronaviridae family, the Orthocoronavirinae subfamily. The Orthocoronovirinaea subfamily is classified into four genera and a number of subgenus under these genera: Alpha, Beta, Gamma and Deltacoronavirus genera. Viruses under these breeds can be found in humans, bats, pigs, cats, dogs, rodents and poultry (in domestic and wild animals).
The disease spectrum caused by Coronavirus in humans can range from simple colds to severe acute respiratory syndrome (Severe Acute Respiratory Syndrome, SARS). It can cause clinical manifestations in humans and animals with various degrees of respiratory, enteric, hepatic, nephrotic and neurological involvements. With the combination of Sanger sequencing, Illumina sequencing and nanopore sequencing, the first complete genome of the new genus Coronaviruses (COVID-19) was identified and three different strains were identified in bronchoalveolar lavage fluid samples. This virus has the typical features of the Coronavirus family and is located in the Betacoronavirus 2b line. The genomes of these strains and Betacoronaviruses have been shown to be closely related to bat SARS-like Coronavirus isolate Bat-SL-CoVZC45 (Figure 3).



Şekil 3: Yeni *Coronavirus*'un filogenetik ilişkisi (*Tan W , Zhao W, Ma X, et al. A Novel Coronavirus Genome Identified in a Cluster of Pneumonia Cases — Wuhan, China 2019−2020, Notes from the Field, China CDC Weekly*)

The virus responsible for COVID-19 is located under the Sarbecovirus subspecies in the genus Betacoronavirus, which it contains in SARS-CoV and MERS-CoV. The new nomenclature of the virus has been accepted as SARS-CoV-2.)

4.6 Turkish Beam Therapy Study of Viral Source

The Mechanism of Viruses
Corona (crowned) Viruses

The mechanism of damage caused by SARS-CoV in cells, tissues and organs is still not fully understood. SARS-CoV must protect itself from the immune system of host cells in order to effectively replicate and reproduce. The virus, by escaping from the natural immune cells of the living creature it infects, negatively affects the mRNA of the host cell through nsp1 proteins, and seizes the metabolism of the host cell by modulating the host's ubicutination pathway with nsp3 proteins. After viral replication occurs in the host cell, cell damage is caused by viral-induced cytolysis or immunopathology. In studies, intestinal biopsy specimens of SARS patients have been detected by electron microscopy, viral factors as well as minor cytopathic effects or inflammations [11].
In transcriptome profiles of infected Caco-2 epithelial cells, a marked increase in strong immunosuppressive cytokine transformation growth factor β and antiapoptotic host cellular response

was observed. Again, in samples from infected animals (non-inflammatory secretions, diarrhea and feces), a large amount of viral factors were detected. The clinical or histopathological findings in the organs or tissues of the host cell are not only dependent on the presence of the relevant receptor and nucleus receptors or viral efficiency reflected by the viral load, but also in the determination of the inflammatory and apoptotic responses of the cell triggered by the virus, the regeneration power or functional reserve of the infected organ, the findings and the outcome of the infection. reported to be important [11].

In a study, it was stated that nsp1 expression in human lung epithelial A549 cells can increase the expression of chemokines (IP10, CCL3 and CCL5) in the NF-κB pathway. IP10 of chemokines expressed on pneumocytes; it has been observed to be a potent chemoattractant for active cytotoxic T lymphocytes, natural killer cells, and monocytes, causing infiltrations in the lungs of SARS patients and interstitium and alveoli [12].

SARS-CoV dominates the lungs with simultaneous activation of proinflammatory chemokines and cytokines in the case of suppressing the IFN-β / α in type 2 pneumocytes without activating the natural immune response and IFN-induced genes and thus performing an uncontrolled viral replication in the cells. It has been reported to be in the position and be fatal [11].

In another study, it was found that the early induction of IP-10 and IL-2, as well as the overproduction of IL-6 and the lack of IL-10 production contributed to the immuno-pathological processes due to lung damage in SARS [13] . For these reasons, it is a known fact in many studies that chemokines produced by infected organs cause adaptive immune disorders and immune cell infiltrations in the lungs [14].

Source, Ways of Infection, Symptoms and Diagnosis

Source

It has not been clarified yet.

The origin of SARS-CoV-2 is still under investigation. Available data indicate wild animals illegally sold in the Huanan Seafood Wholesale Market.

Infection

The disease is transmitted mainly through droplets. In addition, it is transmitted to the droplets produced by sick individuals by coughing and sneezing, after they come into contact with the hands of other people, bringing their hands to the mouth, nose or eye mucosa and touching them.

The virus can be detected in the respiratory secretions of asymptomatic individuals, but the main infection is from the sick individuals. When the epidemiological characteristics of the cases in China were examined, it was observed that in some cases where the average incubation period was 5-6 days (2-14 days), it could extend up to 14 days.

The infectious time of COVID-19 is not exactly known. It is thought that it starts 1-2 days before the symptomatic period and ends with the disappearance of the symptoms.

Coronaviruses are generally viruses that are not very resistant to the external environment. There is a residence time that varies according to the humidity and temperature of the environment, the amount of organic substance it is expelled, and the texture of the surface it contaminates. It is generally accepted that it loses its activity within a few hours on inanimate surfaces. When interpreting the activity time on inanimate surfaces, it should be kept in mind that not only the activity of the virus continues, but also the duration of the contact.

Today, the contamination time and the duration of the external environment of COVID-19 are not known clearly. (Covid-19 guide T.R.Ministry of Health, March 23, 2020)

The first symptom of the disease is usually (> 38 C) high fever *(15,19)*. In addition, feeling of restlessness, chills, sore throat, cough, muscle pain, pneumonia, diarrhea (10-20%), shortening of breathing depth or difficult breathing are among the most observed symptoms *[16,19]*.
While radiological findings are normal in the early stages of the disease, consolidated areas due to focal interstitial infiltrates are detected in lung x-rays taken later on [16]. Leukopenia is observed in patients, while the decrease in lymphocyte numbers is noteworthy, lactate dehydrogenase, creatine phosphokinase and transaminase levels may increase. In addition to these findings in the future, most patients develop thrombocytopenia, that is, the number of blood platelets may decrease.
The disease may be subclinical in some people, as well as in severe and lethal form in people with weakened immunity (children and elderly people) or diabetic people. People with complications such as hepatitis are also at higher risk for serious complications [11, 17, 19].
For the diagnosis of SARS-COV, blood samples, nasal / throat cultures, stool and sometimes urine or tissue samples tests from patients should be studied in laboratories with biosafety level 3 (BSL-3) (11,19). PCR tests performed with reverse transcriptases (RT-PCR) specifically targeting the corona viruses specific ORF 1b or nucleoprotein gene, antigen tests with monoclonal antibodies or monospecific polyclonal antibody against N protein and various serological and immunofluorescent tests performed in fluorescent dyes in the laboratory. These are the basic tests used for diagnosis [11]. The immunological tests used for diagnostic purposes are less sensitive than RT-PCR, but they are known as very sensitive and specific tests in both methods [11]. Immunofluorescent antibody (IFA) tests. its biggest disadvantage is that it can give false results in the initial stage of the disease. However, these tests are still used as screening tests that are very effective and fast, especially after the 5th day of infection (11; 16).

Infection Control and Isolation

Isolation measures should be continued during the period in which the patient is in the health facility, since the virus excretion time and infectious time are not known today.
COVID-19 is thought to be of zoonotic origin, and human-to-human transmission is shown in the latest data. For this reason, standard, droplet and contact isolation measures should be taken in cases where the presence of COVID-19 is considered.
Hospitalization:
• Possible cases are followed up in 2nd and 3rd level hospitals.
• The finalized cases are followed in the 2nd and 3rd stage hospitals or in the hospitals designated in the province.
• Patients who need intensive care from the cases that are finalized are followed up in isolation rooms in the 2nd and 3rd level intensive care units.
Standard infection prevention and control measures should be applied in healthcare facilities. In addition, the application of contact and droplet protection measures should be continued until the patient becomes asymptomatic.
The following infection prevention and control measures should be applied to prevent the spread / transmission of the disease at the health facility.
As the personal protective material required for personnel who will come closer to 1 meter closer to certain / possible COVID-19 cases;

1. Gloves,
2. Gowns (non-sterile, preferably liquid impermeable and long sleeves),
3. Medical mask (surgical mask),

4. At least N95 / FFP2 mask (Only during the process causing droplet / aerosolization) *,
5. Face Guard,
6. Glasses **,
7. Liquid soap,
8. Alcohol based antiseptic,

Sufficient amount should be kept available by inpatient health institutions.
It can be used by making decisions on the basis of overalls, bones and foot protectors, especially in cases where intensive contact with the patient's body fluids and secretions can occur.

Recommendations for the use of Personal Protective Equipment

https://hsgm.saglik.gov.tr/depo/covid19/rehberler/covid_table_hsgm.pdf?type=fil to
* Process that causes droplet / areosolization; aspiration, bronchoscopy and bronchoscopic procedures, intubation, respiratory tract sampling
** Reusable glasses are cleaned according to the manufacturer's recommendation. If there is no special recommendation, it should be disinfected with 70% ethyl alcohol and left to dry on its own in an appropriate environment. In case of using the glasses again, the health institution is instructed where the glasses will be removed, stored and disinfected.

Treatment Methods

In the treatment of SARS-CoV, corticosteroids, which affect the whole body, which is known as the immune modulator treatment method, and have anti-inflammatory and immunosuppressive effects, ensure early recovery of the fever and more harmless radiographic leaks. Ribavirin, which is the nucleoside analogue used in treatment, is known as an agent that has antiviral activity against many DNA and RNA viruses. Ribavirin blocks the viral replicase polyprotein and stops RNA replication. Another method used in the treatment of SARS-CoV is the protease inhibitor (18,19).
Lopinavir-ritonavir common formulation, which is also used in the treatment of HIV infection, can be used in conjunction with ribavirin in the early stages of the disease, and may help antiviral therapy (18,19). However, additional research is needed to develop new treatment methods such as additional antiviral treatments, RNA silencing methods, anti-monoclonal antibody, anti-viral peptides and vaccines, as well as the use of interferon and general steroids in the treatment of immune-mediated lung injuries (16,19).
COVID-19 Outpatient Clinic or Emergency Admission and Follow-up (for cases aged 16 and over)
Patients from the triage-orientation area are evaluated in terms of COVID-19 case definition, with the mask attached.
-COVID-19 fits into the definition of the case, are taken to the specified area.
- Appropriate personal protective equipment (gown, medical mask, goggles / face protector, gloves) are entered in the area where the patient is located.
- The patient's anamnesis is taken,
- Inspection is done
Vital findings are checked (heart rate, rhythm, respiratory rate, blood pressure, body temperature and oxygen saturation are checked if conditions are appropriate)
- The patient's general condition is unstable; respiratory and circulatory support is provided and hospitalized to the relevant service *,
- The patient, whose condition is stable, is examined
- Inspections are requested; - Blood tests:
Complete blood count, Urea, creatinine, sodium, potassium, chlorine, AST, ALT, total bilirubin, LDH, CPK, D-dimer, troponin, C-reactive protein values may be requested when the doctor deems it appropriate.
- Imaging: A chest X-ray is taken and evaluated, and Lung CT is taken with the appropriate technique in the following described situations.

- Clinical decision should be made according to the history and examination findings in pregnant patients who cannot have CT.

Lung BT:

1- Fever + cough - Chest X-ray natural: Low-contrast CT without contrast

2- Fever + cough - Chest X-ray diagnostic / not diagnostic: Low-dose CT without contrast

3- Fever + cough + comorbid disease or advanced age (60 years old and above) + non-diagnostic chest radiography: Full-dose CT without contrast, contrast CT is taken if there is indication for another disease

1- Uncomplicated disease table

a. No underlying disease (cardiovascular diseases, DM, HT, cancer, chronic lung diseases, other immunosuppressive conditions)

b. Having symptoms such as fever, muscle / joint pain, cough, sore throat, nasal congestion

c. Patients with normal pulmonary film and / or pulmonary tomography

A respiratory sample is taken for testing using personal protective equipment for COVID-19.

It is sent to the isolation areas or home designated by the Provincial / District Health Directorate to monitor symptoms with isolation suggestions outside the hospital, and their daily follow-up is done by phone.

If the test is positive, the patient is hospitalized and oseltamivir and hydroxychloroquine are started. If it turns out negative; If the disease is resolved, act according to alternative diagnosis. Patients who have a negative test but worsen symptoms are called to the hospital for re-evaluation. To rule out COVID-19, a second respiratory tract sample is taken and the test is requested. It continues to be followed up, inpatient or inpatient, depending on the clinical condition of the patient.

2-Pneumonia / Those that fit the definition of severe pneumonia

I.

a. Respiratory rate <30 / minute, SpO2 level above 90% in room air and

b. Patient with signs of pneumonia on chest radiograph or tomography

It is deposited in the relevant service. A respiratory sample is taken for COVID-19. The test is done. Without waiting for the test result, oseltamivir and hydroxychloroquine are started in accordance with the treatment algorithm. The test result is followed.

II

a. It has a follow-up (≥30 / minute) with SpO2 level below 90% in the room air,

b. Patient with signs of pneumonia or developing acute organ dysfunction on chest X-ray or tomography

deposited in the intensive care unit. A respiratory sample is taken for COVID-19 and the test is performed. Without waiting for the test result, oseltamivir and hydroxychloroquine are started in accordance with the treatment algorithm. The test result is followed.

If the test results are positive; the result is notified to the Provincial Health Directorate and acts according to the case management scheme.

If the test results are negative;

If there is worsening of clinical findings in outpatients, the test is repeated.

If no alternative diagnosis can be made in patients who are hospitalized, the test is repeated.

* If there are the following intensive care indications in the hospitalization process, the patient is admitted to the intensive care unit and to the relevant service in other conditions.

. Intensive Care Unit Hospitalization Indications:

- Respiratory rate ≥ 30
- Dyspnea and breathing difficulties findings

- Cases with oxygen saturation below 90% despite nasal oxygen support of 5 liters / minute and above
- Cases with partial oxygen pressure below 70 mmHg despite nasal oxygen support of 5 liters / minute and above
- PaO2 / FiO2 <300
Lactate> 4 mmol / L
Bilateral infiltrations or multi-lobar involvement on chest x-ray or tomography
- Hypotension (systolic blood pressure <90 mmHg,> 40 mmHg drop from usual SKB, mean arterial pressure <65 mmHg)
- Skin perfusion disorder
Organ dysfunction such as kidney function tests, liver function test disorder, thrombocytopenia, confusion
Presence of immunosuppressive disease
- The presence of more than one disease at the same time
- Troponin height, arrhythmia
(Covid-19 guide T.R.Ministry of Health, March 23, 2020)
Given all these issues,
The treatment method we developed with the UVC method, especially affects the nucleic acids in the DNA and RNA chains of bacteria, fungi and viruses, disrupts the connective structure and inactivates the pathogens that cause infection. The Ultraviolet-C (UVC) beam used is an alternative to alternative methods to existing methods used in the treatment of localized infections. The inactivation mechanism of UVC is accomplished by providing dimerization of microorganisms to the genetic material in the nucleus or pyrimidine molecules in the nucleic acids in the virus. Thus, the proliferation of nucleic acids (microorganisms) is inhibited and inactivated. The UV-C spectrum, especially the range of 250-270 nm, is strongly absorbed by the nucleic acids of a microorganism and at the end of this process it performs its breakdown.

4.7 Selective Permeable Effective Ultraviolet Wavelength Determination to be Applied

The ultraviolet C (UVC) beam is an alternative methods to existing methods used in the treatment of localized infections. Some drug resistant microorganisms have also been found to be sensitive to UVC irradiation. UV radiation can kill all kinds of microorganisms with its short wavelength and high energy. The greatest antimicrobial activity is in the wavelength region of 250-264 nm.

Contrary to what is known, UVC, selected with appropriate doses, can selectively inactivate microorganisms while maintaining the viability of mammalian cells and has also been proven to promote wound healing. UVC (200nm - 280 nm) has been proven to cause less damage to tissue than UVB in animal studies. [one]. Although UVC can cause DNA damage in mammalian cells, it can be quickly repaired by DNA repair enzymes. [one]. In summary, UVC is an innovative treatment method of our age as an alternative approach to existing methods used for localized infections, single stranded RNA and double stranded DNA viruses, especially for the treatments caused by highly antibiotic-resistant microorganisms. UVC should be used in such a way that side effects are minimized and the resistance of microorganisms to UVC is prevented.

4.8 Benefits / Risks:

Risks from implementation:
-Vascular rupture
-If the guide cannula moves out of the target, tissue damage and radiation-related damage
-Depending on the place of application, thrombosis
-Pulmonary tissue damage
-Pnomotoraks
-Hemotoraks

Risks from the beam device:
Retinal damage and vision loss

The risks mentioned above are due to the fact that the work team is selected from experienced and competent people.
has been minimized. They will also undergo a separate training for applications. Already intensive care and intubation in intratracheal / pulmonary / intravascular interventions
In addition to the risks that may occur under the
It stands out.
On the other hand, it is compulsory to use ultraviolet-proof glasses as specified in the protocol for the patient who performs the application. There is no additional risk that may arise from the device.
However, the benefit that will arise from beam application is very high compared to these risks.
With the treatment we envisaged, survival will increase significantly.
We think that the duration will be shortened and superinfections will be prevented. Summarized benefit / risk
we estimate that the rate is very high and the risk is minimal

5.0 METHODOLOGY

5.1 Patient Admission Criteria (Diagnosis / Medical Table)

Symptoms such as fever, weakness, cough, mild shortness of breath between the ages of 40-75 referring to the clinic with COVID-19 (SARS-CoV-2) test positive or atypical in CT findings. Patients with signs of pneumonia and considered COVID 19, undergoing intubation treatment in the intensive care unit, and meeting the inclusion / exclusion criteria. Patients who are not found suitable according to the intervals specified in the Inclusion / Exclusion criteria will not be included in the study.

5.2 Inclusion Criteria

- Respiratory rate ≥ 30

- Dyspnea and breathing difficulties findings

- Cases with oxygen saturation below 90% despite nasal oxygen support of 5 liters / minute and above

- Cases with partial oxygen pressure below 70 mmHg despite nasal oxygen support of 5 liters / minute and above

- PaO2 / FiO2 <300

Lactate> 4 mmol / L

Bilateral infiltrations or multi-lobar involvement on chest x-ray or tomography

- Hypotension (systolic blood pressure <90 mmHg,> 40 mmHg drop from usual SKB, mean arterial pressure <65 mmHg)

- *Skin perfusion disorder*

Organ dysfunction such as kidney function test, liver function test disorder, thrombocytopenia, confusion

Presence of immunosuppressive disease-

Presence of uncontrolled comorbidity with more than one feature
- Troponin height, arrhythmia
- COVID 19 Test positivity

5.3 Exclusion Criteria

- *Under 40 years old*
- *Pregnant women and those with suspected pregnancy*
- *Those with a history of anaphylaxis*
- *Those with known DNA repair deficiencies:*
- *Those diagnosed with mental disorder,*
- *puerperant women and lactating women*

5.4 Applied Treatment

5.4.1. Treatment Definition and Method

The system should be inserted into the Invamed Steerable Catheter (disposable CAMERA CATHETER) via an ultraviolet / laser light source and the fiberoptic cables connected on it. Ultraviolet / laser light from the end of the fiberoptic system destroys microorganisms (including viruses) at the end of a second-long application. The system is based on the basis of the elimination of microorganisms in these areas with a low dose of UV light / laser application from the catheter by sending it directly to the body cavities via a fresroptic catheter, intrarespiratory, intravascular (used with intracat). With the help of Invamed Steerable Catheter (Disposable Camera Catheter), UVC beam applied with a catheter inserted into the lungs and accompanying fiberoptic are interventions related to the reduction or elimination of infection. With the application of ultraviolet light / laser beam, the patient is treated with a significant reduction / destruction of the microorganism and inflammation burden in the patient's body. The proposed treatment is an antimicrobial treatment strategy, and it is recommended to combine supportive treatments with this process in terms of a holistic treatment strategy based on the clinical course of the disease. UVC and Laser application will be performed on the research arm, together with intravascular and intrarespiratory application.

Effective Dose: *The blood / tissue infected with microorganism, the effective dose required to destroy the microorganism population: 2 mj / cm2* ***[4]***

5.4.1.1. Intravascular UVC Application Process Steps:

- Hands are washed in accordance with the "Hand Hygiene and Glove Directions for Use".
- The patient is given a position in which he / she can feel comfortable according to the application area.
- A protective cover is placed under the interference area.
- Sterile Gloves are worn. IV cannula outer cover is opened.
- Fiberoptic catheter system is slowly pushed into the IV cannula.
- Approximately 5 cm cut from the tip of the catheter is adjusted to remain in the intrvascular area and UVC application is started.
- The Fiberoptic catheter is with drawn slowly after UVC administration at the specified time and strength.
- In order to apply the energy required for microorganism inactivation with the power value applied with UVC source, 200 mj / cm2 energy should be applied for 30 minutes +/- 5 minutes.

b. Open System Intratracheal UVC Application Process Steps:

- Hands are washed in accordance with "Hand Hygiene and Glove Usage Instruction",
- Endotracheal UVC application should be done with two people whenever possible. If the application is to be made by one person, the sterility of the hand, especially the fiberoptic line and the steerable (disposable camera catheter) catheter, should not be impaired.
- Disposable sterile gloves should be worn and the sterility of the fiberoptic line and the glove in the hand where the steerable catheter will be kept should be maintained.
- The ventilator hose should be hung so that it does not touch anywhere after leaving the patient.
- The sterile gloved hand should be pulled from the fiberoptic catheter package and wrapped around the hand to prevent contamination.
- Steerable Catheter should be gently advanced through the endotracheal tube
- Fiberoptic line should be advanced slowly.
- When the Steerable Catheter reaches the carina (resistance is felt and the patient usually coughs), progression should be stopped and the Steerable Catheter should be withdrawn about 1 cm.
- Afterwards, the catheter should be rotated slowly and should be gently advanced towards the pulmonary main bronchus on the side desired to be reached.
- If the patient needs a second UVC application, a separate sterile catheter should be used.
- The time required for the tracheal application of the energy required for the microorganism inactivation with the power value applied by the UVC source, these values are indicated in the table below according to the trachea diameter. **(Table 1).**

Respiratory Application Diameter Mm	Power Per Unit Area	Application time	Energy Required
Diameter (mm)	mw/cm^2	s	mj/cm^2
5	67,90	2,95	200
10	61,11	3,27	200
15	57,72	3,47	200
20	55,00	3,64	200
25	52,28	3,83	200
30	49,57	4,03	200
35	46,85	4,27	200
40	44,14	4,53	200

45	42,10	4,75	200
50	40,74	4,91	200

(Table 1)

Depending on the trachea diameter in the drawn CT, force should be applied for the time specified in the relevant table. The amount of energy to be transferred to the tissue is arranged according to the table with each advance of the fiberoptic catheter 1 cm.

c. Orotracheal / Nasotracheal UVC Application Process Steps:

- Hands are washed in accordance with "Hand Hygiene and Glove Usage Instruction",
- The patient is given a semi-fowler position, the head is brought into a hyperextension state,
- If orotracheal UVC application will be applied, airway is placed,
- The patient is given 100% oxygen for 2 minutes,
- Sterile gloves are worn,
- Steerable catheter is advanced through the airway to the orotracheal region in accordance with the aseptic technique.
- Fiberoptic UVC is advanced through the line catheter in accordance with the aseptic technique.
- When the catheter inserted through the nose or mouth reaches the pharynx, the patient is coughed and the catheter is advanced in the inspiratory phase and UVC is applied.
- The patient is monitored throughout the procedure,
- After the procedure, the patient is given 100% oxygen for 1 minute.
- The time required for the tracheal application of the energy required for the microorganism inactivation with the power value applied by the UVC source, these values are indicated in the table below according to the trachea diameter. **(Table 1).**

Respiratory Application Diameter Mm	Power Per Unit Area	Application time	Energy Required
Diameter (mm)	mw/cm^2	s	mj/cm^2
5	67,90	2,95	200
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20	55,00	3,64	200
25	52,28	3,83	200
30	49,57	4,03	200
35	46,85	4,27	200
40	44,14	4,53	200
45	42,10	4,75	200
50	40,74	4,91	200

(Table 1)

Depending on the trachea diameter in the drawn CT, force should be applied for the time specified in the relevant table. The amount of energy to be transferred to the tissue is arranged according to the table with each advance of the fiberoptic catheter 1 cm.

The healthcare personnel who receive the treatment, taking into consideration the clinical condition of the patient, should not exceed the maximum application time (30 min +/- 5 min in intravascular applications, 5 min +/- 1 min in intrarespiratory applications), and this should be at most 5 days. should apply in accordance with the protocol.

CLINICAL WORK TREATMENT AND FOLLOW-UP PROGRAM								
Evaluation	**Screening Visit (Day 0)**	**Inclusion / Randomization (Day 0)**	**Treatment Visit (Day 1)**	**Treatment Visit (Day 2)**	**Treatment Visit (Day 3)**	**Treatment Visit (Day 4)**	**Treatment Visit - Final (Day 5)**	**Label Period / Follow-up Visit (Day 7&15)**
Informed Volunteer Consent Form	X							
Demographic information	X							
Medical history / General physical examination	X	X	X	X	X	X	X	X
Current treatments (drugs)	X	X	X	X	X	X	X	
Biochemistry, Complete blood count	X	X	X	X	X	X	X	X
Radiological Imaging	X	X		X			X	X
Vital findings	X	X	X	X	X	X	X	X
Include / exclude criteria		X	X	X	X	X	X	
Pregnancy test (serum / urine)	X	X						
randomization		X						
Dose diary			X	X	X	X	X	
Adverse Event		X	X	X	X	X	X	X
Concomitant Therapy (UVC)			X	X	X	X	X	X
PCR sampling			X		X		X	X
Serum Antibody Level								X

Following the improvement of the clinical course of the patients, it is planned to take the patient's serum plasma on the 7th and 15th days, and to test and store it under suitable conditions for the antibody test.

Blood tests to be performed: Complete blood count, urea, creatinine, sodium, IL-1 β, IL-6, TNF α, TGF β potassium, chlorine, AST, ALT, total bilirubin, LDH, CPK, D-dimer, troponin, Ferritin , fibrinogen, procalcitonin, CRP values, quantitative measurement of PCR results of the source of infection

Radiological Imaging: Chest X-ray and / or Lung CT is taken. Clinical decision should be made according to history and examination findings in patients who cannot have chest X-ray and / or lung CT. (Radiological findings: Consolidation, ground glass appearance and reticulo-nodular opacity

appearance should be investigated in lung CT. Signs of pneumonia in lung graphy should be examined.)

5.5 Primary Endpoints

- Ending the vital functions of the patient (medically accepted ex)

Or

- Gloskow Coma Level 13 and above,
- At least 3 days body temperature must have remained normal (measurement from the ear 37.5 C)
- Respiratory symptoms should be significantly improved
- The nucleic acid test must be negative in 2 consecutive tests for the respiratory pathogen (sampling interval must be more than 24 hours)
- Obvious healing of lesions with CT
- There should be no comorbidity or complications requiring hospitalization
- Without oxygen support SaO2 should be> 93%

All of its items have been realized

5.6 Secondary Endpoints

- Hypersensitivity
- Temporary shortness of breath
- Rarely, redness of the skin is due to heat
- Edema
- Bleeding
- Embolization
- Hematoma
- Hyperpigmentation
- Ache
- paresthesia
- Superficial thrombophlebitis
- May cause urticaria or ulcers.
- Vascular rupture and perforation
- Visible scratch
- Iatrogenic injury may damage the surrounding tissues.
- Hemothorax or pneumothorax.
- Neighboring Nerve Damage Iatrogenically
- phlebitis
- Skin Burn or discoloration

If two or more adverse effects from the above adverse effects are seen, the study is terminated.

6. Statistical Evaluation:

According to the course of the clinical trial, if we reach the research arm (100 patients), control group (100 patients), the efficacy and safety of the treatment will be examined and an interim report will be prepared. According to the results of the interim report, the clinical trial will be terminated or the clinical trial will be continued until the number of volunteers (400 in total) mentioned above is completed.

In this interim analysis, the patients completing the study will be evaluated considering the primary and secondary endpoints stated in the protocol and the criteria are as follows:

1-Duration in intensive care
2-Survival rate
Contribution of UVC and laser beam application to the treatment of 3-COVID 19 infection and / or superinfections accompanying COVID 19 infection

The tests to be applied are as follows:
1-Difference test between two averages for intensive care stay
(Mann-Whitney U test or t test) will be used.
2-Survival analysis tests will be used for survival rate.
Accompanying 3-COVID 19 infection treatment and / or COVID 19 infection
To investigate the contribution of UVC and laser beam application to the treatment of superinfections
Chi-square test will be applied.

Descriptive statistics will also be given for demographic data.

REFERENCE STUDIES ABOUT THE APPLICATION OF UVC BEAM "in vitro, in vivo and ex vivo"

1. The Effect of UV-C Ray Reducing Pathogen Rate on Blood Platelets Apps;
- Auto-immune diseases HIV 1 -2
- T-lymphotropic virus types 1 and 2
Hepatitis B (HBV)
Hepatitis C (HCV)
Hepatitis A and E
- Blood pathogens (Treponema pallidum)
- Parvovirus B19

With reference, UVC application, application procedures were made to reduce the amount of pathogen by preparation procedures of existing blood platelets. Platelet samples were irradiated with UV light at a wavelength of 254 nm in plastic bags (transparent) made of polyolefin acetate, and the total UVC doses applied were adjusted by irradiation time. A 1 minute irradiation time of approximately 0.4 J / cm2 was applied from both sides and the results were evaluated by two-dimensional gel electrophoresis.

Gram-positive (B. cereus, S. Aureus and S. Epidermidis) and Gram-negative bacteria (E. Coli, K. Pneumoniae, P.Aeruginosa) bacterial inactivation with UVC treatment, 5

log with dosing at 0.4 J / cm2 this dose with reduced titer; found equally effective for: [2].

Sterilization of bacteria-loaded platelets; No bacterial growth was observed with a concentration of (100 CFUs / mL) cultured for 5 days, with the dose of S. Aureus and S.epidermidis 0.4 J / cm2 at a dose of [2].

UVC study of blood platelets for 7 different virus types
Tested using single-stranded (ss) RNA or DNA viruses, with or without envelopes, as well as suid herpesvirus (SHV) -1, a double-stranded (ds) DNA virus. With a slight dose of 0.4 J / cm2, the titer was reduced by 3.53 log. SHV-1 has been observed to be more resistant to UVC treatment [2].

Being more vulnerable to UVC irradiation, tested;
Small viruses (whether with or without envelopes), a decrease of 0.4 J / cm2, from 0.4 log (WNV) to 0.4 log (VSV and PPV).
HIV (a small ssRNA virus) has been observed to decrease the infectivity of this UVC dose by 1.4 log [2].

Microbiocidal and virusidal properties of UV irradiation have been known for a long time. In addition, shortwave UVC light (wavelength range 200-280 nm) has already been used for pathogen inactivation in serum, plasma and blood products such as albumin, intravenous immunoglobulins and Factor VIII concentrates [10].

Like all other pathogen inactivation methods, the advantage of the UVC technique is undoubtedly the absence of photosensitive compound, and therefore even the receiver of inactivated PCs is not exposed to a chemical compound trace. Clinically relevant G (+) and G (-) bacteria and small non-enveloped viruses are effectively inactivated. In addition, it minimizes the risk of transmission of protozoa such as Tripanosoma cruzi and Leishmania infantum and effectively inactivates Babesia divergens. The UVC method is effective for leukocyte inactivation, including T cells responsible for TA-Gvhd. Therefore, when patients at risk of developing TA-GvHD need PC transfusions, UVC irradiation is sufficient and no additional irradiation (with radiators) is required. In addition, pilot studies show that UVC irradiation not only inhibits cytokine synthesis, but also protects receptors against antigen alloimmunization. However, there are limitations such as low activity against HIV (only 1 day reduction) and increased secretion of platelet chemokines. [10].

2. Inactivating hepatitis C virus in donor lungs using light therapies during normothermic ex vivo lung perfusion

A significant number of organ donors are in the risk group for hepatitis C virus (HCV) infection. Here, studies have been carried out to evaluate the reliability and effectiveness of UVC rays in lung transplantation, where the risk of HCV transmission of UVC beam applied to the lungs before transplantation has been minimized significantly. [3].
The presence of organs is a limiting factor for lung transplantation and leads to significant mortality rates on the waiting list. The use of organs from donors with infectious viral infections such as hepatitis C virus (HCV) will increase organ donation, but these organs are generally not recommended for transplantation due to the high risk of contamination. Here, a method for the treatment of HCV infected human donor lungs that prevents transmission of HCV has been studied. In combination with germicidal light-based treatments, physical viral clearance

inactivates the HCV virus in a short time during normothermic ex-vivo Lung Perfusion (EVLP), a method for the evaluation and treatment of injured donor lungs. This treatment has been shown to be safe using a large animal EVLP-lung transplantation model. The strategy of treating viral infection in a donor organ during protection can significantly increase the availability of organs for transplantation and promote further clinical development. [3].
The UVC lamp (OSRAM Puritec® HNS 4W G5, 254 nm) or customized LED light source (centered emission at 660 nm) is placed inside the quartz tube, depending on the treatment. irradiated, UVC treatment (254 nm, 31 mW / cm², irradiation time 8 hours) applied to perfusate (flow 1 L / min) [3].

3. lnactivation of three emerging viruses - severe acute respiratory syndrome coronavirus, Crimean-Congo haemorrhagic fever virus and Nipah virus.:- in platelet concentrates by ultraviolet C light and in plasma by methylene blue plus visible light

In this study, the effectiveness of UVC beam on DNA and RNA viruses such as corona virus, crimean-congo and nipa virus, which are accepted as pandemics, were investigated. It has been observed that virus effectiveness has been made inactive by application at the rate of 20J / m2. As a result of this examination, when the samples loaded and not loaded with bacteria were examined, it was understood that the observed decrease was completely caused by UVC and MB light. The effectiveness of UVC light against single chain RNA coronavirus has been observed [4].

4. Prevention of viral transmission during lung transplantation with hepatitis C-viraemic donors: an open-label, single-centre, pilot trial
It has been observed that by using UVC light for 4-6 hours before EVLP, HCV curvature is significantly reduced in the first 7 days after transplantation. This study suggests that it may be possible to develop new strategies for routine use in clinical practice for the HVC-positive lung transplant procedure. A significant proportion of organ donors are in the risk group for hepatitis C virus (HCV) infection, where studies have been conducted to assess the safety and effectiveness of UVC rays for transplantation of the lungs, to prevent transmission of HCV to the donor organs through organ transplantation. It was able to prevent contamination. [6].

5. *Potential ln Vivo UVC Disinfeclion of Catheter lumens: Estimation of the Doses Received by the Blood Flow Outside the Catheter Tip Hole*

Using UVC light sources, such as antiseptic lamps for disinfection of blood products, therapeutic treatment of whole blood and the treatment of human body or implant-related infections: Mohr and others have developed a method of pathogen inactivation for blood products using UVC irradiation. Under constant shaking with blood, he exposed it to UV light in a UV-permeable bag. They concluded that an exposure dose of 500 J / m2 resulted in an acceptable disinfection rate in their solution without sacrificing the quality of platelets. At 1500 J / m2, in vitro UVC (254 nm) irradiation of the platelet suspension layer caused a decrease in the number of platelets. UVC irradiation in biological systems has a large number of effects. The inactivation of UVC viruses and bacteria is also based on this mechanism [7].

6. *Ultroviolet C lrradiation for Prevention of Centrol Venous Catheter-related lnfections: An in Vitro Study*

With the long-term use of central venous catheters in the body or vein, a biofilm layer is seen in which microorganism development occurs between the catheter surface and the vessel wall. The

application of 254nm UVC beam applied with the help of a fiberoptic in the catheter lumen with the help of a power source has proven to significantly decrease the microorganism population (grampositive bacteria, gramnegative bacteria, fungi) present on this surface. When applying to the central venous catheter inner lumen for 60 seconds with an energy of 3.6 Joule during application, 99% microorganism inactivation was achieved. [8].

7. *Ultraviolet-C Light for Treatment of Candida albicans Burn Infection in Mice*

In this study, the use of 254nm UVC light was investigated for the treatment of Candida Albicans infection in third degree burns in mice. As a result of testing UVC on mouse skin, no serious damage was observed in the skin tissue and it was concluded that there was an increase in the loss of fungal lumenscence. It was concluded that UVC light therapy was effective on mice with this infection. [5]. Candida albicans is the most common fungal pathogen responsible for fungal infection in burn patients, and is the fourth most common organism found in blood cultures in intensive care unit patients.
In the light of the different in vitro, in vivo and ex vivo studies performed to date, the basis of this research project prepared is mainly based on the nucleic acids of bacteria, fungi and viruses that affect the nucleic acids in the DNA chains and inactivate the pathogens that cause infection.

Documents

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- *SG5/N2:2007 Clinical Evaluation*
- *SG5/N3:2010 Clinical Investigations*
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PROTOCOL APPROVAL

Study Code: MD2020/001

Study Title: Prospective, Parallel, Multicenter Randomized Controlled Study Investigating the Effects of UVC Beam and Laser Beam Therapy According to Standard Therapy in Patients with Covid-19 Diagnosis

Coordinator
Name Surname: Hikmet Selçuk GEDIK Signiture: