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Photodynamic Therapy

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Regarding Ultraviolet blood irradiation, sepsis and antibiotic resistant pathogens:

As a Principal Investigator at the Wellman Center for Photomedicine, at Massachusetts General Hospital and Harvard Medical School, I have researched how light affects human biology, and studied light therapy for various diseases over the last 30 years. My colleagues and I have produced over 350 peer-reviewed research papers and I have personally edited or written the main textbooks used in the study of light and medicine.

My colleagues and I recently produced a review that was published on February 3, 2016 entitled, "The Cure That Time Forgot". This review examined a modality called Ultraviolet Blood Irradiation (UBI). A process, which uses UV light and blood as a therapy for a range of serious diseases.

The following is my opinion of the technique and my examination of its safety and of a certain device that has just passed its European CE medical device certification. This device is now available for further studies and is presently available on the European market. In general, it has great potential to quiet the cytokine storm in sepsis and effectively treat some of the ESKAPE pathogens.

It is my opinion that this device should be welcomed as a potential candidate to treat the above disorders. It is safe, it has been very effective in the past and it should be seriously considered for IRB approved clinical trials by many institutions. The device can be seen at www.ultraluxuv.com

It is appropriate to repeat what I said the end of the review paper. *"We would like to propose that UBI be reconsidered and reinvestigated as a treatment for systemic infections caused by multidrug-resistant Gram-positive and Gram-negative bacteria in patients who are running out (or who have already run out) of options. Patients at risk of death from sepsis could also be considered as candidates for UBI."*

Sincerely,

Michael R Hamblin, Ph.D.
Associate Professor

Safety of UV blood irradiation (UBI)

History. UBI is often known as “the cure that time forgot” [1, 2]. UBI was extensively used in the 1940s and 1950s to treat many diseases including septicemia, pneumonia, tuberculosis, arthritis, asthma and even poliomyelitis [2-12]. Hundreds (if not thousands) of lives were saved in the days before antibiotics. The early studies were carried out by several physicians (including Emmett Knott, George Miley, and Robert Olney) in USA and published in the highly respected journal “American Journal of Surgery” [3, 13, 14]. However with the development of antibiotics in the 1950s, the use of UBI declined, and at present in the USA its use is confined to alternative and complementary medicine practitioners.

The introduction of the Salk vaccine against poliomyelitis also took attention away from UBI, which had actually shown good results against polio [6]. The early pioneers established that there was an optimum proportion of the total blood volume (circa 5%) that should be irradiated with UV light. Higher proportions produced less benefit, and irradiating the entire blood volume was fatal to dogs.

Modern practice. The modern practice involves removing a relatively small sample (40-60 mL out of 5.5L total) of blood from a vein, adding heparin to prevent clotting, diluting it with 160 mL of sterile saline and placing the diluted blood in a bag connected to a tube that delivers the blood to the proprietary cuvette. The cuvette contains a turbo-rotor that ensures the flowing blood is exposed to the UV light at the surface of the tube cuvette.

The UV light is produced by three distinct wavelength lamps within the device (UVC 254nm power 1X), (UVB 280-330nm power 2X), and UVA (330-370nm power 3X). As the diluted blood is passed through the cuvette at a rate of 10ml/minute, it is simultaneously reinfused into the patient and finally any remaining blood in the system is returned. All components are certified sterile and medically qualified professionals are present throughout the procedure.

The experience of over 200,000 human treatments has not yet uncovered any serious adverse effects. It should be noted that this therapy has been in continual use for the last 50 years. In the past poor flow characteristics of the cuvette and weak and single light sources were common. Even with these sub-optimal devices there were remarkable, documented therapeutic benefits. The weaknesses of the older devices seem to have been overcome with the newer devices like the UltraluxUV.

There has been one study in the **International Journal of Infectious Disease - 2015 Aug;37:58-63** completed with a more complex device but using similar wavelengths. <https://www.ncbi.nlm.nih.gov/pubmed/26092299> [15]

Here is their conclusion:

In this study, UVBI was safe and had a beneficial effect in the treatment of HCV. This device should be studied for use in psoriasis and in infectious diseases that have few treatment options.

The “medical” indications for UBI are many and various and include the following:

Viral Infections: (Hepatitis, Influenza, Herpes, Mononucleosis, Viral Pneumonia, Shingles);

Bacterial Infections: (Pneumonia, Wound Infections, Septicemia, Peritonitis, E. coli, Glanders, Lyme disease, Tetanus);

Inflammatory Conditions (Arthritis, Fibrositis, Bursitis, Nephritis, Iritis, Uveitis, Cholecystitis, Pancreatitis);

Circulatory Conditions: (Peripheral vascular disease, Deep Vein Thrombosis, Claudication, Thrombophlebitis);

Autoimmune Disorders: (Lupus, Rheumatoid Arthritis, Psoriasis, Multiple Sclerosis);

Respiratory Disorders: (COPD, Asthma, Emphysema, Sinusitis, Bronchitis).

The skepticism that clearly surrounds UBI today can be attributed to three principal causes.

- First, any therapy that can treat such a diverse array of diseases and conditions, appears to be simply “too good to be true”, and is therefore probably “snake-oil”.
- Second, there is no consensus on the scientific principles underlying the mechanism of action.
- Third, there have been no well-controlled (double blind, randomized, placebo-controlled) clinical trials, at least in Western countries in recent years.

Mechanisms of action. It is commonly assumed that the mechanism of action of UV blood irradiation must involve some UV mediated killing of pathogens. All microorganisms (bacteria, viruses, fungi and parasites) are exceptionally sensitive to the effects of UV. However the fact that only a relatively small percentage of blood requires to be treated (circa 1-5%) does not logically agree with this hypothesis. Moreover the ability of UBI to treat disorders with no infectious etiology (such as autoimmune disorders) also does not agree. We believe that the mechanism of action involves the UV light interacting with components of the blood (proteins and cells). It is likely that many different blood components are affected - monocytes, lymphocytes, erythrocytes, dendritic cells, neutrophils, and even proteins such as lipoproteins and immunoglobulins may be affected. The net result is that there is a significant decrease in inflammation (important for patients with sepsis and inflammatory conditions) and the natural antimicrobial activity of the host cells is markedly increased. Another common observation is that the oxygen carrying capacity of the blood is increased, which is beneficial for many respiratory diseases.

Requirements for Significant Risk (SR) device

Under 21 CFR 812.3(m), an SR device means an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

If the device (and the study) does not pose a serious risk then it can be classified as a non-significant device and coupled with a study.

In order to assess this device and the corresponding study as a non-significant risk one needs to look at the potential hazards of UV light radiation on blood.

Possible theoretical hazards

1) UV light can cause cancer. Although UV light can clearly act as a carcinogen (especially in skin) it needs to be chronically applied over a surprisingly long time in the absence of any genetic disease involving defective DNA repair systems. It is thought to cause mutations in tumor suppressor genes such as p53. However there are two very good and separate reasons why the use of UBI cannot cause cancer.

(A) It would have needed to be repeated many, many times (possibly tens and more likely hundreds of times) to stand any chance of causing cancer even if such were possible.

(B) In order to cause cancer, mutations need to be caused in stem cells or progenitor cells such as are found in epithelial structures (skin, intestine, lung, prostate etc) or lymphoid organs (bone marrow, lymph nodes), or mesenchymal tissues (muscle, bone). There are no stem cells or progenitor cells circulating in normal blood, therefore the concept of carcinogenicity cannot apply.

2) Adverse host reaction against UV-damaged blood components. It might be thought that there might be an adverse reaction of the host to some component of the blood that has been damaged by UV light. The simple loss of (even all the living) cells in such a small amount of blood (40-60cc) would not cause any harm, and it must be remembered that blood cells die all the time (particularly lymphocytes and neutrophils that undergo apoptosis very efficiently).

3) Adverse reaction with concurrently administered drugs present in the blood. It might be claimed that UV light could interact with a medicinal or pharmaceutical compound that is already in the bloodstream to produce a toxic reaction product. However it should be remembered that only 1-2% of blood volume (and hence only 1-2% of the drug present in the body) is treated, and the penetration of the UV light into the cuvette is unlikely to be sufficient to carry out UV-mediated photolysis.

Conclusion

Taking into account all the foregoing considerations I believe that it is clear that the UltraluxUV UBI system does not present “a potential for serious risk to the health, safety, or welfare of a subject.”, and should therefore be declared a non-significant risk device. My hope is that there will be clinics and medical institutions that will take up the challenge of proving the efficacy (or non-efficacy) of this device through some clearly-defined IRB-approved clinical trials.

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