Tying the past to the present: time tested knowledge with state-of-the-art technology in the fight against emerging and drug resistant microbes

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Reka Szigeti and Richard Kellermayer

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Correspondence to:
Reka Szigeti
Department of Pathology and Genomic Medicine, Houston Methodist Hospital, 6565 Fannin, Houston, TX 77030, USA
Department of Pathology and Immunology, Baylor College of Medicine, Houston, TX, USA
rszigeti@houstonmethodist.org

Richard Kellermayer
Section of Pediatric Gastroenterology, Texas Children's Hospital, Baylor College of Medicine, Houston, TX, USA USDA ARS Children's Nutrition and Research Center, Houston, TX, USA

Multidrug-resistant and emerging novel microbes impose a huge burden to modern medicine. The sensitivity to ultraviolet (UV) light of many of these organisms is well known and thoroughly characterized. As an example, UV irradiation is a well-established method for viral inactivation in transfusion medicine,[1] either by itself (UVC) or in the presence of riboflavin (UVB) or amotosalen (UVA), and even visible light may be effective in the presence of methylene blue.[2–4]

UV-sensitive viruses can cause deadly diseases, such as Ebola or members of the *Coronaviridae* family, among many others. Ebola is highly sensitive to UVC radiation,[5] and a critical step in Ebola infection is its replication in monocytes and vascular endothelial cells that leads to extreme viral loads in patient blood.[6] Additional examples are Coronaviruses, which are highly UV sensitive[3] and were the etiological agents of three severe respiratory syndrome outbreaks. These outbreaks include the current coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is dramatically affecting and claiming lives around the globe. Recent studies on SARS-CoV-2 showed that the level of viremia/RNAemia may correlate with disease progression.[7–9] One of the first reports from Chen *et al.*[7] indicated that the 2019-nCoV (i.e. SARS-CoV-2) RNA was readily detected in the blood in six of 57 (i.e. 10.5%) patients. Importantly, all six patients with detectable viral RNA in the blood progressed to severe symptom stage, suggesting a strong correlation between serum viral load and disease severity (p-value = 0.0001). An observation by Hogan *et al.*[8] on COVID-19 patients found that SARS-CoV-2 RNAemia in plasma occurs more commonly (32.1% *versus* 14.0%; $p = 0.05$) in individuals with severe disease, who required intensive care unit (ICU) transfer. These findings are consistent with those during the SARS epidemic. The median concentration of serum SARS RNA was found to be 26–30-fold higher at hospital admission in those patients requiring ICU care, compared to those who did not.[9] Consequently, plasma localized viruses, such as Ebola and Coronaviruses as examples, may serve as therapeutic targets for UV irradiation in blood-disseminated infections.

Beyond viral pathogens, emerging multidrug-resistant organisms (MDROs) (usually bacteria) are frequently sensitive to UV radiation.[10] Some estimates indicate MDRO-related sepsis to be the third most common reason for death in the United States, for example.[11] Many MDRO sepsis cases occur in transiently immunocompromised patients, such as during and after chemotherapy or bone marrow transplantation. It is during such septic episodes, when MDROs can become therapeutic targets for UV irradiation as well.

We propose that the level of viremia/bacteremia and consequently the systemic spread of many infections could be decreased by variable modes of UV irradiation, through treating of the patient's plasma by plasmapheresis combined with extracorporeal antimicrobial UV irradiation. This treatment modality may be sufficient to attenuate the disease adequately until effective seroconversion or immunological recovery can occur. The specific duration and frequency of the treatment will need to be tailored to the particular infectious organism and the patient's condition.

This treatment option has surprisingly not been considered for patients with viral/bacterial/fungal sepsis caused by UV-sensitive microorganisms. 'UV-exerted antimicrobial plasmapheresis' would treat the patient's extracorporeally separated plasma in a real-time fashion, similar to, but distinct from extracorporeal photopheresis, in which the separated buffy coat is treated.[12] As opposed to extracorporeal photopheresis, our proposed method treats only the plasma in a real-time fashion and leaves cellular blood components unaffected. This could be achieved by creating a closed system plasmapheresis. Namely, a UV transparent reservoir would be incorporated in the plasmapheresis circuit, which would be exposed to UV light. Once the plasma (that may contain already developed neutralizing antibodies against the particular pathogen, which would be preserved by this technique) is adequately irradiated to inactivate the microorganism by UV (based on already available sensitivity data),[3] it would be directly circulated back into the patient in this closed system. Importantly, this methodology: (a) could be used for both mono, and polymicrobial infections if the infectious agent(s) are UV sensitive; (b) would allow for the preservation of serum proteins and antibodies during UV irradiation;[1] (c) could be used in combination with other therapeutic measures; and (d) is essentially readily available in advanced medical settings.

In conclusion, we propose a novel, but clinical trial ready, safe approach to attenuate UV-sensitive microorganisms in blood. This intervention carries the potential to significantly increase survival in deadly viral and bacterial infections.

Author contributions

RS: conceptualization, data curation, writing-review-editing; RK: conceptualization, data curation, writing-review-editing.

Conflict of interest

A patent related to this work is pending.

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ORCID iD

Reka Szigeti https://orcid.org/0000-0002-8650-1265

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