Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Can charcoal improve outcomes in COVID-19 infections?

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ABSTRACT

COVID-19 infection causes considerable morbidity and mortality, especially to those who are aged, have impaired renal function and are obese. We propose to examine the potential utility of oral activated charcoal with the hypothesis that such treatment would lower absorption of microbiome derived toxins and ameliorate systemic oxidant stress and inflammation.

Background to hypothesis

While coronaviruses have been known to cause potentially serious disease for ½ a century [1], COVID-19 has created a pandemic with adverse health consequences beyond the experiences of those people living today. As of July 14, 2020, approximately 13 million people have been infected with at least 570,000 dying from this disease and its complications [2]. Interestingly, the range of signs and symptoms ranges from those who have essentially no symptoms to those with fatal disease. It appears that age, renal dysfunction and obesity are amongst the most important risk factors for serious or fatal COVID-19 infection [3,4]. While there are multiple mechanisms by which this virus can injure hosts, it appears that increases in systemic cytokines and widespread inflammation may play an important role [5].

Our research group has focused on the role that adipocytes play in the pathophysiology of metabolic and CV disease. In particular, we have noted that in experimental models of these diseases, the redox state within adipocytes has profound consequences to systemic oxidant stress, inflammation and disease phenotype [6–9]. We have specifically identified that products derived from tyrosine and tryptophan which are produced by the intestinal microbiome, specifically p-cresyl sulfate and indoxyl sulfate can directly cause oxidant stress in adipocytes [10]. These substances are excreted by the kidney and are known to accumulate in the plasma with impaired renal function [11]. Some workers have hypothesized that the symptoms of uremia itself can be modulated by use of oral activated charcoal to lower absorption of these microbiome products [12]. Experimental data also support the concept that uremia potentiates sepsis and that oral activate charcoal can attenuate this [13].

On this background, the adipocyte is a known target for the virus [14], and as people age there are statistically likely decreases in renal function and increases in visceral adipocity [15]. There are data suggesting that the virus can induce oxidative stress in adipocytes [16] and this oxidative stress can upregulate the expression of the ACE-2 protein [17], the putative receptor for COVID-19. In short, the elderly likely have increases in the circulating concentrations of these potentially toxic substances as well as the adipocyte mass which responds to them [16].

Hypothesis

Administration of activated charcoal has been shown to be well tolerated when administered to a patients with renal dysfunction [18,19]. This activated charcoal has also been shown to effectively decrease circulating levels of p-cresyl sulfate and indoxyl sulfate [13]. In addition to its ability to scavenge these microbiome derived toxins, activated charcoal may also have non-specific absorptive properties that blunt inflammatory responses to [20] or possibly inactivate viruses [21]. Certainly, COVID-19 infection may directly involve the gastrointestinal tract in both human and bat [22]. Given that the potential toxicity of oral activated charcoal is so limited, we propose that an investigation of this coal-derived substance, widely available in the "mountain" state of WV, to potentially attenuate these adverse outcomes be explored as definitive work seeking effective antivirals and development of a vaccine continues. A schematic summarizing this hypothesis is shown in Fig. 1.

To test this hypothesis, we would suggest first a proof of concept study where a relatively small group of patients at high risk for COVID-19 complications are given activated charcoal at doses similar to that used in previous renal failure studies [18,19] when the diagnosis is first made. Cytokine levels, concentrations of indoxyl sulfate and p-cresyl sulfate along with evidence for systemic oxidant stress (e.g., protein

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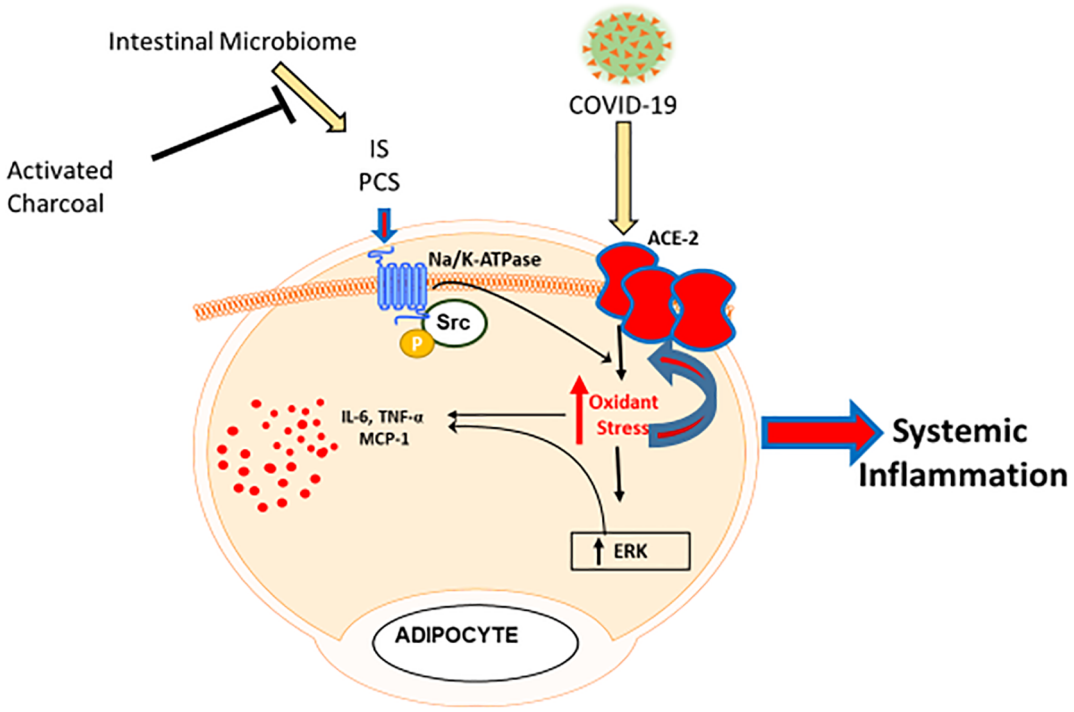

Fig. 1. Schema demonstrating intestinal microbiome-induced activation of Na/K-ATPase oxidant amplification loop in adipocytes exacerbating inflammation in COVID-19 infections. The microbiome causes increases in indoxyl sulfate (IS) and p-cresyl sulfate (PCS) absorption which, in turn, activate Na/K-ATPase signaling. This results in feed-forward amplification of ROS and cytokine production along with an alteration in the adipocyte phenotype. These ROS also increase ACE2 expression, facilitating COVID-19 adipocyte infection which exacerbates this process. These effects would be attenuated by activated charcoal effecting decreases in microbiome-derived IS and PCS absorption.

carbonylation) and inflammation would be serially monitored. Should preliminary outcomes be improved with this strategy, a randomized, prospective blinded study should be performed prior to large scale adaptation of this treatment strategy.

Contributions

JIS: Put forward the central hypothesis.

ZJK, IK, MAM, JRS, NGA, SVP, US, JIS: Participated in drafting and finalizing the paper and in literature search.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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