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Response

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Keywords

ARDS; therapeutic hypothermia; neuromuscular blockade

Dear Drs. White, Ghamande, and Arroliga,

We appreciate the positive comments of White et al. (1) and the recent contribution from their group to the limited body of literature about therapeutic hypothermia (TH) in the management of ARDS (2). We agree with all comments made about the outstanding questions relevant to how, when, and whether to use TH in patients with ARDS. It is not yet clear whether TH would be add-on or replacement for the limited therapeutic options currently available. However there is evidence that lower temperatures can directly modulate some signaling pathways that are central to the pathogenesis of ARDS, including p38 MAPK (3) and TRPV4 (4). Furthermore, since TH is more widely available and requires less manpower than ECMO and prone positioning it may be a less expensive and more widely achievable therapeutic option. However, shivering and its metabolic consequences are known to be a major adverse event during TH (5). To begin to answer the question of whether TH is safe and beneficial in ARDS, we are planning a Phase IIb randomized clinical trial (RCT) of TH in patients with ARDS who are receiving neuromuscular blockade (NMB) as part of their ARDS management. We reasoned that since all subjects would already be receiving NMB, the ultimate anti-shivering treatment, cooling would be facilitated without need for additional anti-shivering treatment and would simplify a multi-site clinical trial. Our pilot study (6) succeeded in our objectives of demonstrating feasibility of utilizing such patients in a prospective RCT of TH vs. standard temperature management and provided effect size estimates to plan a Phase IIb study using surrogate mortality endpoints.

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