LETTER TO THE EDITOR

Author Response

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Dear Editor,

I would like to extend my gratitude for the opportunity to respond to the letter submitted by the readers.[1] The use of vasopressor therapy in septic shock at high doses, as highlighted, can lead to various complications, and the pursuit of alternative non-adrenergic agents is a commendable approach to mitigate these issues.[2] Intravenous methylene blue infusion can play a crucial role as a non-catecholamine vasopressor therapy in reversing refractory shock.[3] Our study has definitely added to this exploration by examining the potential of methylene blue as a non-adrenergic alternative.

The concern raised regarding the non-significant improvement in lactate clearance alongside MAP improvement is valid. Elevated lactate levels can indicate inadequate oxygen delivery to tissues, leading to anaerobic metabolism.[4] Shock has various causes like sepsis, trauma, heart issues, and low blood volume, each with its own way of causing cellular dysfunction. Treating shock shouldn't just focus on fixing lactate levels; it's crucial to tailor the treatment to address the specific cause or origin of the shock. Furthermore, the resolution of shock may outpace lactate clearance, as it takes time for lactate levels to normalize during tissue recovery.[5] While lactate clearance is a useful tool in managing patients with shock, it should be interpreted in conjunction with other clinical and hemodynamic parameters. Monitoring trends in lactate levels over time can help guide therapeutic interventions, but it should not be viewed in isolation as a definitive indicator of complete tissue perfusion reversal. Other measures, such as blood pressure, heart rate, urine output, and clinical assessment, are also crucial in the overall evaluation of a patient in shock. Despite lactate being an indicator of better tissue perfusion, our research did not show a notable clearance in lactate levels with the use of methylene blue. The lack of a significant improvement in lactate clearance in our study is a crucial factor to bear in mind when interpreting the results. Therefore, further studies are needed to thoroughly evaluate the overall impact of methylene blue on patient outcomes in terms of reversal of tissue perfusion.

The issue of methylene blue responders versus non-responders is an important one. With nearly half of the subjects in the study not responding to methylene blue, it raises questions about the broader utility of this intervention. The effectiveness of methylene blue may vary depending on the type of shock, being more successful in certain cases and less so in others. Patient-specific factors, encompassing comorbidities, baseline health, and organ dysfunction severity, can impact how individuals respond to treatment with methylene blue.[6] The efficacy of methylene blue infusion in reversing refractory shock is most pronounced when initiated promptly at the onset of refractory shock.[7] However, a significant limitation of our study is the inability to specify the optimal time frame for initiating methylene blue infusion. Consequently, a substantial portion of our study population did not exhibit a positive response to the therapy. I concur with the readers' suggestion for a more pragmatic approach, which involves comparing patients undergoing methylene blue treatment to those receiving conventional therapy without any methylene blue intervention. Such a study design could shed more light on the true efficacy of methylene blue as a rescue measure in refractory shock.

While our study does show promising signs in correcting macro-circulatory parameters, it also raises important questions regarding the complete reversal of shock, the response rates, and the utility of methylene blue in addressing tissue hypoxia. I acknowledge the call for more comprehensive studies to further investigate the efficacy of methylene blue and other novel therapies in managing the complex pathophysiology of refractory shock.

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