LETTER TO THE EDITOR

Methylene Blue in Septic Shock—A Novel Weapon in Our Arsenal: Are Utility Studies Highlighting its Futility?

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Dear Editor,

We read the article by Rajbanshi et al., on the use of intravenous methylene blue, recently published in September issue of IJCCM.[1] Refractory shock being a common issue in ICU patients, we attempt to critically analyze this topic in the light of available evidence.

Vasopressor therapy in septic shock at high doses is often associated with numerous complications such as tachyarrhythmias, increased myocardial, oxygen consumption, etc.[2] Numerous nonadrenergic agents such as hydrocortisone, vasopressin (and its synthetic analogs), and angiotensin II have been tried as rescue measures.[3] Targeting the root pathophysiology in late stages of shock, therapies centered around antagonizing the vasodilatory effect of nitric oxide—one of the primary mediators of vasorelaxation in septic shock, have received significant attention.[4] The study by Rajbanshi et al. is yet another venture toward testing the efficacy and effectiveness of another nonadrenergic drug – methylene blue, as compared with conventional vasopressor therapy.

Cryptic shock, i.e., hyperlactatemia with normal-appearing hemodynamic variables, represents occult global tissue hypoxia and possibly impaired microcirculation. Though traditionally considered as a premonitory stage of shock, the outcomes for these patients are as bad as in those with overt/hypotensive shock.[5] Serum lactate is an important indicator of tissue hypoperfusion, and its clearance has been suggested as a therapeutic target in the management of septic shock. Rajbanshi et al. did not find a significant improvement in lactate clearance to accompany the improvement in MAP. Can we truly regard this as complete "reversal of shock"?

In the index study, the two cohorts for comparison were (1) methylene blue responders vs (2) methylene blue nonresponders. Nonresponders constituted 46% of the total subjects enrolled in the study. The implication, when extrapolated to a larger cohort of patients, would be that nearly half of them would not be responsive to methylene blue in the first place, let alone its utility in correcting tissue hypoxia. With the nonresponse rate amounting to approximately 50% to the first dose of methylene blue, would it qualify as a pragmatic intervention based on this study design? A realistic study design would be to compare cohorts of patients who receive methylene blue vs conventional therapy (do not receive even a single dose of methylene blue).

We appreciate the authors' effort in testing this novel therapy. Having shown signs of improvement in correcting the "macrocirculatory parameters" (indicators of overt shock), the study definitely shall encourage more effort in this regard. With emphasis on addressing the oxygen demand–supply mismatch in shock, more studies testing the efficacy of methylene blue in this regard would be needed.

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