The Editor,
We have read the interesting study “Methylene Blue for Postcardiopulmonary Bypass Vasoplegic Syndrome: A Cohort Study.”[1] We appreciate the authors for conducting one of the largest observational studies of methylene blue administration for vasoplegic syndrome in cardiac surgery patients. However, we would like to add a few points to the study.

First, in the author’s study methylene blue was administered in a dose of 1–2 mg/kg bolus over 10 min and the median time until a maximum hemodynamic response was 2 h after drug administration. Out of 88 patients who received methylene blue, only 39 (44.3%) showed a positive hemodynamic response to the drug. We believe that if the bolus of methylene blue was followed by a continuous infusion of the drug, it would have produced even better results. Evora et al. have reviewed 20 years of vasoplegic syndrome treatment in heart surgery and found that the most used dosage of methylene blue is 2 mg/kg as an intravenous bolus, followed by the same dose in continuous infusion because its plasma concentration sharply decreases in the first 40 min.[2,3]

Second, while comparing the variables associated with methylene blue response, the authors did not take into account the dose of protamine given to neutralize heparin in the study population. It is very likely that the vasoplegic syndrome in these patients was due to the high dose of protamine which then responded to a single bolus dose of methylene blue. Viaro et al. studied the intrinsic mechanism of protamine vasodilation was nitric oxide/cyclic guanosine monophosphate-dependent and endothelium-mediated. They suggested methylene blue as a novel approach to prevent and treat hemodynamic complications caused by the use of protamine after cardiopulmonary bypass (CPB).[4]

Third, the authors did not measure serum lactate levels in response to methylene blue treatment. The authors have mentioned in the limitations of their study that the target means arterial pressure at their Intensive Care Unit was 70–80 mmHg, which could be variable at different centers. We believe that measuring serum lactate levels in response to methylene blue would also be a good indicator of its hemodynamic effects. In a study by Leyh et al., 54 patients with norepinephrine-refractory vasoplegia after CPB were treated with methylene blue (2 mg/kg) administered intravenously over 20 min. They found a significant decrease in arterial serum lactate concentration within 24 h after starting methylene blue infusion, underlining the restoration of normal peripheral blood flow after methylene blue infusion.[5] Maslow et al., in their randomized control trial, studied the hemodynamic effects of methylene blue when administered at the onset of CPB. In their study, 30 patients taking angiotensin-converting enzyme inhibitors within 24 h before elective heart surgery were randomized to receive either methylene blue or saline during CPB. They found that lactate levels were significantly reduced in the methylene blue group at all time periods during CPB after administration of the drug.[6]

We acknowledge and appreciate the authors for their in depth study. At the same time, we propose that if the above recommendations were considered, it would have yielded more holistic results.

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Conflicts of interest
There are no conflicts of interest.

Neha Pangasa, Rohan Magoon, Vandana Bhardwaj, Amita Sharma, Ameya Karanjkar, Poonam Malhotra Kapoor
Department of Cardiac Anaesthesia, CTC, AIIMS, New Delhi, India

Address for correspondence:
Dr. Neha Pangasa, Department of Cardiac Anaesthesia, CTC, All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110 029, India. E-mail: nehapangasa@gmail.com

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