Continuous versus intermittent methylene blue administration: which spin will win?

Sir,

The article by George *et al*. is indeed interesting.[1] However, a few aspects of their report require contemplation. The use of methylene blue continuous infusion in the management of methemoglobinemia due to insecticide poisoning is not congruent with current evidence. Methylene blue is a cationic thiazine dye and acts as an oxidant. It has assumed a significant role, with diverse applications in clinical practice, but is fraught with risks of side-effects.[2] Methylene blue is reduced to leukomethylene blue by erythrocyte methemoglobin reductase in the presence of nicotinamide adenine dinucleotide phosphate (NADPH). Further, leukomethylene blue reduces methemoglobin to oxyhemoglobin. Therefore, large doses of methylene blue may result in higher levels of methylene blue rather than the expected leukomethylene blue, which could potentially induce acute hemolytic anemia, independent of preexisting methemoglobinemia.[3] This is strengthened by reports of the paradoxical induction of methemoglobinemia by methylene blue.

The possible mechanisms resulting in rebound methemoglobinemia include continued absorption of the inciting drug as well as prolonged half-life in the setting of renal or hepatic dysfunction.[4] For example, the hydroxylamine metabolites of dapsone responsible for the formation of methemoglobin have a half-life of over 30 h and may linger in circulation for up to 35 days. These agents are metabolized to reactive metabolites that oxidize

hemoglobin. The redox reaction to form methemoglobin regenerates the parent compound, which can then be remetabolized to the oxidative metabolite. Therefore, to prevent the relapse of methemoglobinemia, adequate decontamination with activated charcoal is essential. In addition, dextrose infusion is necessary, to provide adequate substrate to form NADPH, through the hexose monophosphate shunt pathway, which is essential for reducing enzymes to be effective.

The authors have used continuous infusion of methylene blue, to prevent rebound methemoglobinemia. Although there are reports[5] which advocate the continuous infusion of methylene blue to prevent rebound methemoglobinemia, it is prudent to avoid it as standard therapy.[6] The current recommended regimen is intermittent bolus dose of methylene blue for the treatment of methemoglobinemia.

Subramanian Senthilkumaran, Suresh S. David[1], Rishya Manikam[2], Ponniah Thirumalaikolundusubramanian[3]

Department of Emergency and Critical Care Medicine, Sri Gokulam Hospitals and Research Institute, Salem, [3]Department of Internal Medicine, Chennai Medical College and Research Center, Irungalur, Trichy, Tamil Nadu, [1]Department of Emergency Medicine, Pushpagiri Medical College Hospital, Tiruvalla, Kerala, India, [2]Department of Emergency Medicine, University of Malaya, Kuala Lumpur, Malaysia

Correspondence:
Dr. Subramanian Senthilkumaran, Department of Emergency and Critical Care, Sri Gokulam Hospitals and Research Institute, Salem, Tamil Nadu, India.
E-mail: maniansenthil@yahoo.co.in

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