CORRESPONDENCE

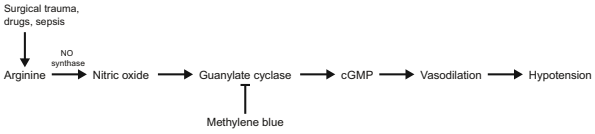
Methylene Blue Is a Guanylate Cyclase Inhibitor That Does Not Interfere with Nitric Oxide Synthesis

To the Editor:

Mangelli and colleagues[1] report the life-saving effectiveness of methylene blue (MB) in treating vasoplegic syndrome in a 75-year-old man, after on-pump cardiac surgery. They present a simplified nitric oxide (NO) pathway that shows methylene blue as a nitric oxide synthase (NOS) inhibitor.

In regard to the therapeutic principles for endothelial vasoplegic dysfunction treatment associated with heart surgery, the first and most important concept concerns restrictions on the use of nonspecific inhibitors of NO synthesis (L - NMMA, L - NAME). This approach is prone to controversy, because it involves ethical issues related to the use of new therapies, besides blocking—not only iNOS, but its constitutive enzyme's (eNOS) organic form.[2,3]

Methylene blue does not interfere with NOS and has played a longstanding beneficial role in many other clinical conditions.[2,3] As a potent guanylyl cyclase inhibitor, MB blocks the release of cyclic guanosine monophosphate (cGMP), thereby preventing vascular smooth muscle relaxation without directly affecting NO synthesis. Nitric oxide synthase inhibitors are not currently in clinical use because of their lack of specificity in inhibiting the different NOS isoforms, with the consequent risk of generalized tissue necrosis and a higher death rate. Therefore, we suggest a modification of the diagram, to avoid restrictions upon MB on the basis of NO's detrimental microcirculatory effect:



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References

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This letter was sent to Dr. Joshua Manghelli, who responds in this manner:

To the Editor:

Dr. Evora is indeed correct that methylene blue inhibits guanylate cyclase[1]; however, there are data to support the contention that it inhibits nitric oxide synthase as well.[2] We believe that the figure should be adjusted to include the inhibition of both enzymes.

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1. Evora PRB. Methylene blue is a guanylate cyclase inhibitor that does not interfere with nitric oxide synthesis. Tex Heart Inst J 2016;43(1):103.
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