Letters to the Editor

The Editor welcomes submissions for possible publication in the Letters to the Editor section that consist of commentary on an article published in the Journal or other relevant issues. Authors

- Include no more than 500 words of text, three authors, and five references
- Type with double-spacing
- See http://jtcs.ctsnetjournals.org/misc/
 ifora.shtml for detailed submission instructions.
- Submit the letter electronically via jtcvs.editorialmanager.com.

Letters commenting on an article published in the JTCVS will be considered if they are received within 6 weeks of the time the article was published. Authors of the article being commented on will be given an opportunity to offer a timely response (2 weeks) to the letter. Authors of letters will be notified that the letter has been received. Unpublished letters cannot be returned.

Methylene blue revised *To the Editor:*

Recently, Taylor and Holtby¹ have presented a case of refractory hypotension in a child with native mitral valve endocarditis with cerebral complications in whom methylene blue (MB) was less effective than previously described.^{2,3}

We have been using MB to treat refractory vasoplegias since 1994, and our experience is corroborated by the specialized medical literature. Most of our experience involved adults who had hypotension during cardiopulmonary bypass (CPB) or after the operation, situation in which, like sepsis, nitric oxide plays a primordial role. 4.5 In this milieu two prospective and randomized studies reached positive conclusions about the efficacy of MB to treat or prevent the vasoplegic syndrome in patients having cardiac surgery with the aid of CPB.

Recently, we operated on a drug-addicted young man with native aortic valve endocarditis. The patient received a bileaflet valve prosthesis (St Jude Medical, Inc, St Paul, Minn). A high dose of norepinephrine was necessary to maintain a reasonable blood pressure during CPB. After weaning from CPB he was hypotensive and had a high cardiac output, low systemic vascular resistance, and pulmonary edema. The arterial oxygen saturation was below 80%, even though he was being ventilated with 100% oxygen and positive end-expiratory pressure. We started MB in a continuous infusion in a way quite similar to that used by Dr Taylor, followed by a bolus of 3 mg/kg (in 100 mL of 5% glucose in water) twice a day. Even though the mean arterial pressure did not increase, even with norepinephrine, the cardiac output gradually decreased, and the systemic vascular resistance increased. In addition, the rapid resolution of lung edema resulting in higher arterial oxygen saturation was astonishing.

Although Drs Taylor and Holtby seemed disappointed with the effect of the MB on blood pressure, we believe that their case had an impressive evolution despite of its severity. We disagree that "obvious clinical

improvement using MB was not evident in this case," since most of the pharmacologic support to the circulation was necessary for a short time. In our opinion, the controversy about the use of MB to treat similar cases arises when one uses MB merely as a kind of "last-minute vasopressor." MB sometimes seems to work for this purpose and sometimes it does not, perhaps due the fact that, unlike many vasopressors, MB does not act through a membrane receptor. We believe the pivotal action of MB is not exclusively the guanylyl cyclase blockage resulting in a reduction in cyclic guanosine monophosphate (cGMP). This blockage also enhances the "crosstalk" between cyclic adenosine monophosphate (cAMP) and cGMP pathways, which facilitates the effect of the cAMP-dependent vasopressors. Many clinical reports in the medical literature, including sepsis treatment, substantiate that the guanilyl cyclase blockage seems to improve the effect of the vasopressors, shortening the length of pharmacologic cardiovascular support. Another quite advantageous effect of MB is its capacity to reduce vascular permeability.^{8,9}

Paulo Roberto B. Evora, MD, PhD
Alfredo José Rodrigues, MD, PhD
Division of Thoracic and Cardiovascular Surgery
Ribeirão Preto Faculty of Medicine
University of São Paulo,
São Paulo, Brazil

References

- Taylor K, Holtby H. Methylene blue revisited: management of hypotension in a pediatric patient with bacterial endocarditis. *J Thorac Cardiovasc Surg*. 2005;130:566.
- Driscoll W, Thurin S, Carrion V, Steinhorn RH, Morin FC 3rd. Effect of methylene blue on refractory neonatal hypotension. *J Pedi*atr. 1996;129:904-8.
- Grayling M, Deakin CD. Methylene blue during cardiopulmonary bypass to treat refractory hypotension in septic endocarditis. J Thorac Cardiovasc Surg. 2003;125:426-7.
- Evora PR. Should methylene blue be the drug of choice to treat vasoplegias caused by cardiopulmonary bypass and anaphylactic shock? *J Thorac Cardiovasc Surg*. 2000;119: 632-4.

- Evora PRB, Levin RL. Methylene blue as drug of choice for catecholamine-refractory vasoplegia after cardiopulmonary bypass. J Thorac Cardiovasc Surg. 2004;127:895-6
- Levin RL, Degrange MA, Bruno GF, Del Mazo CD, Taborda DJ, Griotti JJ, et al. Methylene blue reduces mortality and morbidity in vasoplegic patients after cardiac surgery. *Ann Thorac Surg.* 2004;77:496-9.
- Ozal E, Kuralay E, Yildirim V, Kilic S, Bolcal C, Kucukarslan N, et al. Preoperative methylene blue administration in patients at high risk for vasoplegic syndrome during cardiac surgery. *Ann Thorac Surg.* 2005;79: 1615-9.
- Kirov MY, Evgenov OV, Evgenov NV, Egorina EM, Sovershaev MA, Sveinbjornsson B, et al. Infusion of methylene blue in human septic shock: a pilot, randomized, controlled study. *Crit Care Med.* 2001;29:1860-7.
- Donati A, Conti G, Loggi S, Munch C, Coltrinari R, Pelaia P, Pietropaoli P, et al. Does methylene blue administration to septic shock patients affect vascular permeability and blood volume? *Crit Care Med.* 2002; 30: 2271-7.

doi:10.1016/j.jtcvs.2005.09.007

Reply to the Editor:

We thank Drs Evora and Rodrigues for their interest in our case report and their comments. The clinical improvement as described in the series by Leyh and associates¹ and the case reports by Grayling,² Sparicio,³ and their colleagues, was not evident in our case. Those authors described dramatic improvements in mean arterial pressure with commencement of methylene blue (MB); our patient experienced no such benefit. Norepinephrine, epinephrine, and vasopressin requirements persisted for at least the first 24 hours after the operation in our case. Her treating intensivists believe that her postoperative course was not significantly shortened by the use of MB. The dose used (2 mg/kg at induction of anaesthesia, 2 mg/kg on initiation of CPB, and an infusion of 1 mg/kg per hour for a total of 4 hours) was based on the description by Grayling and Deakin,2 which is longer than that used by others. 1,3

Nitric oxide vasodilation is implicated in both sepsis and the refractory vasoplegia associated with cardiopulmonary bypass (CPB). The different outcomes in the studies of MB in the septic group and our patient may be due to the different pathology and underlying heterogeneity of septic patients. A case report of dramatic improvement after MB in a patient with infective endocarditis refutes this. Evora and Rodrigues describe the "random" efficacy

of MB when used as a "last minute vasopressor." The evidence for use of MB as anything other than the "last minute vasopressor" in such situations does not exist for children. We, therefore, reiterate the need for clinical trials to answer this question.

Katherine Taylor, BMed(Hons), BA, FANZCA former Fellow in Paediatric Anaesthesia The Hospital for Sick Children Department of Anaesthesia 555 University Avenue Toronto, Ontario M5G1X8, Canada

References

- Leyh RG, Kofidis T, Struber M, Fischer S, Knobloch K, Wachsmann B, et al. Methylene blue: the drug of choice for catecholaminerefractory vasoplegia after cardiopulmonary bypass? [see comment]. *J Thorac Cardiovasc* Surg. 2003;125:1426-31.
- Grayling M, Deakin C. Methylene blue during cardiopulmonary bypass to treat refractory hypotension in septic endocarditis. J Thorac Cardiovasc Surg. 2003;125:426-7.
- Sparicio D, Landoni G, Pappalardo F, Crivellari M, Cerchierini E, Marino G, et al.
 Methylene blue for lithium induced refractory hypotension in off-pump coronary artery bypass graft: report of two cases. *J Thorac Cardiovasc Surg*. 2004;127:592-3.
- Faber P, Ronald A, Millar BW. Methylthioninium chloride: pharmacology and clinical applications with special emphasis on nitric oxide mediated vasodilatory shock during cardiopulmonary bypass. *Anaesthesia*. 2005; 60:575-87.

doi:10.1016/j.jtcvs.2005.10.013

Assumed oxygen consumption in the determination of cardiac output in children after cardiac surgery *To the Editor:*

We read with interest the article by Fakler and associates¹ titled "Assumed oxygen consumption frequently results in large errors in the determination of cardiac output." However, we were surprised that our previous article was not cited. We used respiratory mass spectrometry to continuously measure oxygen consumption (Vo₂) and compared these direct measurements with estimated Vo₂ values using 4 equations, including that of Lafarge and Miettinen. We studied ventilated children with congenital heart disease both during cardiac catheterization and in the intensive care unit early after cardiopulmonary bypass surgery.2 We showed an overestimation of Vo2 in children during cardiac catheterization and an underestimation in the postoperative children, with all 4 equations being particularly unreliable in the postoperative group.

As rightly pointed out by Fakler and colleagues, use of assumed Vo₂ will result in large errors in the calculation of hemodynamic variables, such as cardiac output and systemic and pulmonary vascular resistance. This issue becomes particularly important in patients during the early postoperative period, when Vo2 is not only increased as a result of systemic inflammatory response syndrome but is also highly dependent on temperature,3 the use of inotropes and vasoactive drugs,4 and ventilatory manipulation.5 Thus although the conclusions of Fakler and colleagues support our previous observations regarding the use of estimated Vo2 during cardiac catheterization, we believe our data suggest the need for even greater caution in the more highly dynamic hemodynamic milieu of the postoperative cardiac intensive care

Jia Li, MD, PhD
Igor E. Konstantinov, MD, PhD
Glen S. Van Arsdell, MD
Andrew N. Redington, MD, FRCP
Cardiac Program
Hospital for Sick Children
Toronto, Ontario, Canada

References

- Fakler U, Pauli C, Hennig M, Sebening W, Hess J. Assumed oxygen consumption frequently results in large errors in the determination of cardiac output. *J Thorac Cardio*vasc Surg. 2005;130:272-6.
- Li J, Bush A, Schulze-Neick I, Penny DJ, Redington AN, Shekerdemian LS. Measured versus estimated oxygen consumption in ventilated patients with congenital heart disease: the validity of predictive equations. *Crit Care Med.* 2003;31:1235-40.
- Li J, Schulze-Neick I, Lincoln C, Shore D, Scallan M, Bush A, et al. Oxygen consumption after cardiopulmonary bypass surgery in children: determinants and implications. J Thorac Cardiovasc Surg. 2000;119:525-33.
- Penny DJ, Sano T, Smolich JJ. Increased systemic oxygen consumption offsets improved oxygen delivery during dobutamine infusion in newborn lambs. *Intensive Care* Med. 2001;27:1518-25.
- Li J, Hoskote A, Hickey C, Van Arsdell G, Redington A, Adatia I. Hypercapnia improves systemic oxygenation and decreases oxygen consumption and blood lactate levels in children after bidirectional cavopulmonary shunt operation. Crit Care Med. 2005;33: 984-9

doi:10.1016/j.jtcvs.2005.08.014