Letters to the Editor

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Methylene blue revised

To the Editor:

Recently, Taylor and Holtby[1] 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[6] or prevent[7] 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]

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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 associates[1] 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.[4] A case report of dramatic improvement after MB in a patient with infective endocarditis refutes this.[2]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.

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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 associates[1] 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 (Vo_2) and compared these direct measurements with estimated Vo_2 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 Vo_2 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,[1] use of assumed Vo_2 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 Vo_2 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[1] support our previous observations regarding the use of estimated Vo_2 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 unit.

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