Hydroxocobalamin in Vasoplegic Syndrome: Effects of Poor-Adherence to Pharmaceutical Guidelines and Criteria for Use of B-12

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Introduction
Vasoplegic syndrome, a common condition seen after prolonged period on cardiopulmonary bypass (CPB) and liver transplantation, is a serious state of severe hypotension that is resistant to catecholamines. Due to the high mortality rate associated with vasoplegia, there have been growing interests in finding effective therapeutic drugs to manage the hemodynamic effects resulting from the widespread systemic vasodilation involved (1). Methylene blue (MB), which is the current standard therapy used to treat catecholamine-resistant vasoplegia, has been falling out of favor with emerging evidence showing high morbidity, and increased mortality (2). Recently, there have been growing numbers of case reports and a series reporting successful use of Hydroxocobalamin (HyCob) in vasoplegia. Given the enthusiasm surrounding the use of HyCob for this purpose, it is no surprise that the clinical case series of 37 patients published by Shah et al. showed that about 30% of cases involving the use of HyCob in vasoplegic syndrome did not meet criteria for administration. In this retrospective review, we hope to determine if we need to tighten or enhance guidelines for proper use of HyCob in vasoplegia, thereby decreasing the unnecessary exposure of our patients to HyCob and reducing waste of this costly drug.

Methods
We performed a retrospective chart review of 12 patients undergoing cardiac surgery using cardiopulmonary bypass (CPB) and liver transplant between May 30th, 2018 to January 21st, 2020. The age range was between 21 to 84-years old. Criteria for use of B-12 is refractory vasoplegia defined as MAP < 55 mmHg (and CI > 2.5) despite norepinephrine/epinephrine equal to or greater than 0.2 mcg/kg/min (or phenylephrine equal to or above 2 mcg/kg/min) and vasopressin equal to or greater than 0.03 units/min. Dosing use was 5g of CyanokitTM, with option to re-dose an additional 5g, if patient responds to first dose (Maximum dose is 10g).

Results
The total number of patients that properly received B-12 according to proper pharmaceutical guideline was 3/12 (25 percent) of the patients. Four (4/12) patients did not meet criteria for administration of B-12 as they had MAP > 55. One patient did not meet criteria as an infusion of vasopressin was never started. An additional 4/12 cases did not meet criteria based on the maximum infusion guideline for Epinephrine/Norepinephrine which was never achieved prior to B-12 dosing.

The effects of B12 on MAP was very similar to our earlier reports and those reported in the case series by Shah et al. There were 10/12 (83.33%) patients who experienced an increased in MAP by at least 1mmHg at 5 minutes or less. The range of MAP achieved at 5min was 1-26mmHg.

Conclusion
Reasonable biochemical explanations exist for the probable beneficial effects of B-12 in treating vasoplegia. However, future research is needed to elucidate if and how these biochemical mechanisms are causally involved in effective clinical responders and non-responders. Proper guidelines and criteria should be followed prior to administration of B-12 to avoid confounding errors that may result in under- or over-estimation of the effect of the drug.