Vasoplegic Shock: A Summary of Current Standings

Cara Carlos

Cardiovascular Perfusion Program

Quinnipiac University

Hamden, CT

What is Vasoplegia?

Vasoplegic syndrome (VS), also known as vasodilatory shock (VDS), is a well-documented adverse effect of cardiopulmonary bypass (CPB) surgery, often occurring in parallel to systemic inflammatory response syndrome (SIRS). In the early postoperative period following CPB circuit exposure, patients will commonly present with a lack of vascular tone leading to inadequate tissue perfusion and the potential for organ failure. The hypotensive event is coupled with a cardiac output that is within normal limits or even elevated.[1] In its refractory form, this type of maldistributive shock can manifest as a resistance to vasopressors, rendering treatment less straightforward. While multiple therapeutic avenues are currently in practice, more focused research will aid in proper identification, treatment and (most importantly) prevention of vasoplegia.

Vasoplegia has been appreciated in 5-44% of postoperative CPB patients.[3,4,7] Retrospective hospital studies have found a correlation between VS and increased hospital stay, extended ventilator dependence, blood product usage and mortality in CPB patients.[1,4,7] While certain traits within this patient population have been pinpointed as indicative of increasing the likelihood of vasoplegia development, such as the accumulation of comorbidities as well as mean arterial pressure (MAP) upon induction. The occurrence of vasoplegia does not always behave in a predictable fashion.
The presenting parameters of vasoplegic shock are reported to correlate with a MAP of less than 50-70 mmHg and a CVP of less than 5 mmHg, a normal or elevated cardiac index (greater than or equal to 2.5 L/min/m^2), a low peripheral resistance (800-1400mmHg) and persistent vasopressor requirements.[5,6] One of the most challenging aspects of this disorder is identification. Since vasoplegic shock presents in a frustratingly nonspecific manner that can be attributed to a myriad of etiologies, ruling out alternative sources of hypotension is often the suggested route (via double checking a radial artery reading or the correction of a hypovolemia, for example).

The Link Between SIRS and VDS

Several factors are theorized to contribute to the cardiac patient's risk of developing vasoplegia. Immediately upon initiation of CPB, cardiac surgery activates many inflammatory pathways with detrimental effects that propagate long into the postoperative period. Complement, leukocyte, and contact activation result in the release of cytokines, kallikrein, inducible NO and other inflammatory mediators in a snowballing effect that depletes vital molecules such as clotting proteins and ATP. ATP depletion in conjunction with acidosis will disrupt the membrane gradient and render calcium channel-regulated vasoactivity ineffective, even in the presence of catecholamines. Duration of circuit exposure and reperfusion injury are factors that can increase levels of circulating inflammatory mediators and can therefore be categorized as contributors to vasoplegia risk.[1,3]

When blood passes through the synthetic CPB circuit, plasma proteins adhere to the lumen of the circuitry, causing the aggregation of proteins and subsequent molecular changes to occur. The activation of inflammatory and vasoactive molecules such as reactive oxygen species (ROS), endothelins, platelet activators, inducible NO, cytokines and prostaglandins leads to a massive systemic insult that the body struggles to recover from because vital components such as vasopressin, platelets and ATP have been depleted.

Where Has All the Vasopressin Gone?

The depletion of vasopressin can be exacerbated by historical angiotensin-converting enzyme inhibitor (AChI) drugs used preoperatively to control essential hypertension (HTN). Blocking the renin-angiotensin-aldosterone (RAA) pathway, coupled with a procedure that literally bypasses the site of bradykinin metabolism (lungs) can result in loss of vasomotor tone.[5,7] While not a concrete prognostic indicator, the reaction of MAP to bypass initiation, including the degree and duration of a hypotensive change and its responsiveness to vasoactive drugs, can be utilized as a clue to the extent of inflammatory response and whether endogenous vasopressor levels persist at levels adequate enough to compensate.[7] Other factors such as induction duration, history of congestive heart failure (CHF), previous surgeries, increased BMI and the use of bridge devices exacerbate the risk.[1,7] Interestingly, the case demographic with the lowest incidence of vasodilatory shock are aortic cases, perhaps due to the use of DHCA to maintain the patient during repair.[4]

Treatment

Once a hypovolemia has been ruled out or corrected, practitioners turn to pharmaceutical intervention for vasoplegic shock. Instinctually, the first line treatment for this presentation would be a vasoconstrictive agent. But what can be done when vasoplegia proves refractory to vasopressors? Vasopressin supplementation, to replenish depleted hypophyseal stores, given prophylactically preoperatively, or in adjunct to a catecholamine has been shown to decrease the required dosage.[3,4,6] Methylene blue, a direct NO binding competitor, has come into light as a valid option for treating vasoplegia. Success has been reported in preoperative, intraoperative and single post CPB doses; however it has not proved to be of use post onset of organ failure There is also the known drawback of pulse oximetry interference to consider.[1,3,11] Corticosteroids such as methylprednisolone and dexamethasone have also been administered to mitigate inflammatory mediators, reverse the vasodilatory shock state and as an adjunct to reduce the vasopressor dosage via adrenergic receptor upregulation. However the detrimental impact on wound healing is a consideration. Several studies returned data that failed to support an improvement in mortality with intraoperative administration of these steroids, however they were not specifically focused on VDS and it appears more focused research is warranted.[3] Two other studies supported corticosteroid prophylactic use with an observed decrease in hospital stay and decrease in time of mechanical ventilatory dependence.[1] Exploratory therapies currently include vitamin C for anti-inflammatory and microcirculatory reasoning, hydroxocobalamin (for a hypertensive effect), telipressin (the longer-acting vasopressin analog) and angiotensin II (as encouragement for the natural release of vasopressin).[3]

Prophylaxis

In addition to pharmaceutical interventions (preoperative vasopressin treatment and ACE inhibitor discontinuation, for example), other steps can be taken to reduce patient risk. For the perfusionist, the measures taken to mitigate vasoplegia are the same steps taken to minimize the inflammatory response: short pump runs, judicious use of blood products, minimized circuits and careful hemodynamic monitoring of the patient. It is theorized that an additional thirty minutes

of pump exposure time can increase a patient's risk of developing VDS by 38%.[4] With the increased popularity of MICS and off-pump CABG, hopefully fewer patients will be exposed to the risk. Knowing the patient history and predicting how it will impact the pump run will help the operating team to provide the best patient care. In our time, we are sure to see more research on vasoplegic shock that will hopefully uncover more insight into how we can protect and treat patients. Because vasoplegic shock and septic shock share a similar presentation, most of this knowledge is based upon publications for the latter. With the increase in prevalence of bypass surgeries around the globe, we will hopefully see an increase in investigations dedicated specifically to this life-threatening event. In the meantime, let's keep it short, keep it cold and maintain the MAP!

References

1. Omar, S., Zedan A., and Nugent K (2015). Cardiac Vasoplegia Syndrome: Pathophysiology, Risk Factors and Treatment. Am J Med Sci., Jan;349(1):80-8. doi: 10.1097/MAJ.0000000000000341.
2. Hosseinian, L., Weiner, M., Levin, M., and Fischer, G. (2016). Methylene Blue: Magic Bullet for Vasoplegia? Anesthesia & Analgesia, 122(1):194–201. doi: 10.1213/ANE.0000000000001045
3. Shaefi, S., Mittel, A., Klick, J., Evans, A., Ivascu, N., Gutsche, J., and Augoustides, J. (2018). Vasoplegia After Cardiovascular Procedures—Pathophysiology and Targeted Therapy. Journal of Cardiothoracic and Vascular Anesthesia, 32(2):1013-1022. doi: 10.1053/j.jvca.2017.10.032.
4. Fischer, G. and Levin, M. (2010). Vasoplegia During Cardiac Surgery: Current Concepts and Management. Seminars in Thoracic and Cardiovascular Surgery, 22(2):140-144. doi: 10.1053/j.semtcvs.2010.09.007
5. Mekontso-Dessap, A., Houël, R., Soustelle, C., Kirsch, M., Thébert, D., Loisance, DY (2001). Risk factors for post-cardiopulmonary bypass vasoplegia in patients with preserved left ventricular function. The Annals of Thoracic Surgery, 71(5): 1428 – 1432. doi: 10.1016/s0003-4975(01)02486-9
6. Masetti, P., Murphy, S. F. and Kouchoukos, N. T. (2002). Vasopressin Therapy for Vasoplegic Syndrome Following Cardiopulmonary Bypass. Journal of Cardiac Surgery, 17: 485-489. doi:10.1046/j.1540-8191.2002.01002.x
7. Levin M., Lin, H., Castillo, J., Adams, D., Reich, D., and Fischer, G. (2009). Early On–Cardiopulmonary Bypass Hypotension and Other Factors Associated with Vasoplegic Syndrome. Circulation, 120:1664–1671. doi: 10.1161/CIRCULATIONAHA.108.814533
8. Lambden, S., Creagh-Brown, B., Hunt, J., Summers, C., Forni, L. (2018). Definitions and pathophysiology of vasoplegic shock. Critical Care, 22:174. doi: 10.1186/s13054-018-2102-1
9. Truby, L., Takeda, K., Farr, M., Beck, J., Yuzefpolskaya, M., Colombo, P., Topkara, V., Naka, Y., and Takayama, H. (2018). Incidence and Impact of On-Cardiopulmonary Bypass Vasoplegia During Heart Transplantation. ASAIO J.,64(1):43-51. doi: 10.1097/MAT.0000000000000623.
10. Badke, C. M., Marsillio, L. E., Weese-Mayer, D. E., & Sanchez-Pinto, L. N. (2018). Autonomic Nervous System Dysfunction in Pediatric Sepsis. Frontiers in Pediatrics, 6, 280. doi:10.3389/fped.2018.00280
11. Hosseinian L., Weiner M., Levin M.A., Fischer G.W. (2016). Methylene Blue: Magic Bullet for Vasoplegia? Anesthesia and Analgesia, 122(1):194-201. doi: 10.1213/ANE.0000000000001045