Vasopressor Weaning in Patients with Septic Shock

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KEYWORDS

• Sepsis • Septic shock • Vasopressor • Titration • Wean • Hypotension

KEY POINTS

- The authors recommend close monitoring and aggressive titration of vasopressors to maximize both vasopressor treatment and weaning in patients with sepsis.
- The rationale for mean arterial pressure (MAP) greater than or equal to 65 mm Hg is based on the physiologic concept of autoregulation of blood flow, the body's attempt to withhold or divert blood flow to the most critical organs.
- Close monitoring includes narrow alarm parameters for MAP and heart rate to minimize adverse events and facilitate rapid attainment of MAP greater than or equal to 65 mm Hg and subsequent discontinuance of vasopressor therapy.
- Implementation of a weaning protocol inclusive of narrow monitor alarm parameters will decrease the total time and dose of vasopressor therapy, thereby ensuring adequate tissue perfusion with minimal adverse events.

INTRODUCTION

Sepsis is the leading cause of death in noncoronary intensive care units (ICUs) in the United States[1] and the 11th leading cause of death overall.[2,3] More than 750,000 cases of severe sepsis occur annually.[2] Septic shock, defined as the presence of an infection that causes organ dysfunction and adverse hemodynamic changes,[1] results from severe sepsis. This condition carries a mortality rate of 50% to 70% in the ICU setting.[1] Causes of death are multifactorial, but there is strong evidence to

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suggest that the use of vasopressors contributes to complications and overall mortality. Complications associated with vasopressor use include myocardial and splanchnic ischemia.[4,5] Despite the dangerous complications associated with these drugs, the use of vasopressors for sepsis-induced hypotension is critical to maintain adequate blood pressure and tissue perfusion after fluid resuscitation efforts have failed. This article aims to discuss the pathophysiology of sepsis and hypotension, briefly review current guidelines for treating sepsis, detail the pharmacologic actions of vasopressor therapy, and provide literature and discussion to support rapid downward titration of these drugs with close patient monitoring.

PATHOPHYSIOLOGY OF SEPSIS AND HYPOTENSION

The pathophysiology of sepsis informs assessment and treatment decisions. When a bacterial pathogen enters the sterile environment of the body, the inflammatory response is invoked with the release of neutrophils and later macrophages to promote bacterial phagocytosis. These leukocytes release proinflammatory and antiinflammatory mediators to facilitate phagocytosis. Such proinflammatory cytokines as tumor necrosis factor-alpha (TNF-α) and interleukin-1 (IL-1) cause fever, activate coagulation, and increase endothelial permeability to recruit additional macrophages for suppression of bacterial growth.[6] Such antiinflammatory cytokines as IL-10 and IL-1 receptor antagonist also are released to counter the massive inflammatory response and promote homeostasis.[6] If these mechanisms are able to balance each other appropriately, the infectious process is eliminated and tissue repair and healing can occur. However, if the proinflammatory cytokines extend their reach beyond the area of infection, a generalized systemic response is manifested.

Transition from infection to sepsis occurs (**Fig. 1**) when large quantities of proinflammatory cytokines are released into the bloodstream. In addition to leukocytosis, fever, and activation of coagulation and fibrinolysis, TNF-α and IL-1 promote hypotension.[6] The complement plasma protein system is activated to clear the bacterial components from the blood stream. Subsequent antigen-antibody complexes form large proteins that damage the tissues, and low circulating T- and B-lymphocytes contribute to the immunosuppression seen during sepsis.[7] Tissue ischemia develops when microcirculatory lesions formed during the activation of coagulation reduce oxygen delivery. Subsequent endothelial damage triggers the release of reactive oxygen species, lytic enzymes, and such vasoactive substances as nitric oxide.[6] Endotoxin released from bacterial cell walls, TNF-α, and nitric oxide all destroy the mitochondrial matrix within the cell, resulting in cell injury, reduced energy metabolism, and decreased oxygen utilization.[6] Impaired utilization of oxygen causes organ failure in sepsis. Proinflammatory cytokines delay macrophage apoptosis, which prolongs the inflammatory response and increases ischemia and organ failure. Because the cellular injury affects every organ system, patients experience renal, myocardial, pulmonary, hepatic, and nervous system failure.[6]

Nitric oxide release secondary to endothelial damage and endotoxin is the major contributor to hypotension in septic shock because nitric oxide is a potent vasodilator. If vasodilatation is not treated rapidly, cardiac failure may result and lead to further tissue hypoperfusion and multisystem organ failure.[8] The increased endothelial permeability from proinflammatory cytokines causes vascular leakage and hypovolemia.[6]

TREATMENT GUIDELINES FOR SEPSIS

Monitoring tissue perfusion is a key guideline of the Surviving Sepsis Campaign[1] to prevent, assess, and treat rapid deterioration of patient condition. Systematically