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Improving Vasopressor Safety

Introduction

Vasopressors are high-alert medications. Although their use is somewhat restricted, they constitute a mainstay of supportive care in adult and pediatric critical care units for diverse indications (including cardiac surgery, organ donation, traumatic brain injury and other neurological emergencies), as well as in emergency departments and perioperative care environments. Vasopressors are often used in the management of hypotension that accompanies circulatory failure, a condition commonly known as shock. These drugs are not curative—rather, they support the patient while definitive therapy takes effect. More specifically, vasopressors are used to raise blood pressure to facilitate adequate tissue perfusion (thus allowing for sufficient supply of oxygen and other nutrients to reach body cells and to remove metabolic wastes) while the underlying cause of the shock is treated. Vasopressors can save lives, but they are also associated with harmful systemic effects.

The medication incident described in this bulletin indicates opportunities for safer use of vasopressors. The measures taken to enhance patient safety in this particular case are shared, and recommendations for system improvements regarding vasopressor-related communication are presented.

Treatment of Shock with Vasopressors

Shock is not a disease, but rather a common pathway of circulatory failure characterized by multiorgan dysfunction that is associated with a high mortality rate. Although shock and hypotension often coexist and are sometimes mistakenly considered the same problem, they are not synonymous. A low blood pressure value may be normal (and even healthy) in some individuals, but the same blood pressure can lead to tissue hypoperfusion in others. Nonetheless, extremely low blood pressure invariably results in shock.[1]

Depending on the cause of the shock, intravenous (IV) fluids, inotropes, and/or vasopressors may be used to support patients.[2] Vasopressors are medications that induce arterial (and sometimes venous) vasoconstriction, thereby increasing the patient's blood pressure. Some vasopressors also induce stronger and faster cardiac contractions (known as inotropic and chronotropic effects, respectively). Management can be complex and requires consideration of many variables, such as fluid volume status, serum lactate, arterial and venous pH, and the various medications that can affect hemodynamics.

Vasopressors are life-saving medications for many patients, but their associated and numerous harmful systemic effects must also be recognized, including increased myocardial oxygen consumption, intestinal and limb ischemia, modulation of the immune response against infection, and hyperglycemia.[3,4] Furthermore, vasopressors may mask hypotension, and a clinician's recognition that a patient's condition is deteriorating may be delayed if attention is not paid to vasopressor dosing. Vasopressor use necessitates a

delicate balance between minimizing the dose (to reduce side effects) and maximizing tissue perfusion (to prevent end organ damage).

Guidelines issued by the Surviving Sepsis Campaign have recommended a minimum mean arterial pressure (MAP)* of 65 mm Hg for patients in septic shock, based on expert opinion.[5,6] More specific values (i.e., minimum and maximum values) to ensure adequate tissue perfusion without excessive doses of vasopressors are not yet clear, and studies on this topic are in progress.[7,8]

Medication Incident

A man in his 70s was transferred from a community hospital to the intensive care unit (ICU) of a tertiary care hospital with acute respiratory distress syndrome. He had been admitted to hospital 1 week earlier for community-acquired pneumonia. His condition had deteriorated despite treatment with broad-spectrum IV antibiotics. On arrival, the patient was receiving ventilation through an endotracheal tube. His respiratory rate was rapid, irregular, and poorly coordinated with the respirator. Deep sedation and neuromuscular blockade were required, but these measures resulted in profound hypotension. IV fluids and norepinephrine as continuous IV infusion were ordered by the intensivist. The norepinephrine was to be titrated to maintain MAP of at least 65 mm Hg.

ICU staff were unable to achieve the target MAP despite increasing the doses of norepinephrine during the evening. The resident prescribed continuous IV infusions of vasopressin and epinephrine. Overnight, profound malperfusion occurred, along with multiorgan failure, despite the MAP being on target and even above. On arrival in the morning, the intensivist was surprised that he had not been notified of the situation sooner. The care team realized that they lacked a common understanding of the goals of vasopressor therapy. Continuing efforts to stabilize the patient's condition were unsuccessful, and he died a few hours later from refractory shock.

Shared Learning

Following the incident, an ICU interdisciplinary team (consisting of nurses, intensivists, and pharmacists) reviewed vasopressor use for 3 consecutive weeks in several ICUs within the organization. The following opportunities for improvements were identified:

- Facilitating a common understanding of acceptable MAP or blood pressure values and the intended plan of care for maximum dose of vasopressors
- Prompting more frequent reassessments of vasopressor therapy, to ensure the drug remains appropriate once the cause of a hypotensive episode has become clear
- Identifying a common approach to assessing vasopressor efficacy and treatment failure

A 1-page form was designed to be completed by the treating ICU team during daily morning rounds for every patient receiving a vasopressor (excerpts shown in Figure 1). The form was approved by the hospital's medication safety committee and had the following 3 objectives:

- To provide explicit vasopressor dosing targets to ensure consistency in understanding among all team members (i.e., distinguishing between target range and minimal threshold)
- To prompt, at a minimum, daily reassessments of the indication for vasopressors
- To identify an easy-to-recognize trigger for notifying the most responsible physician

*MAP is the average pressure exerted on the arteries. The MAP can be calculated from diastolic blood pressure (DBP) and systolic blood pressure (SBP), taking into account the heart rate. For example, when the heart rate is between 60 and 100/min, the left ventricular chamber of the heart is resting and filling with blood (a process known as diastole) for two-thirds of the time; for the remainder of the time, the chamber is contracting and pumping blood (a process known as systole). Therefore, $(2/3 \times DBP) + (1/3 \times SBP) = MAP$. This equation can also be expressed as $[(2 \times DBP) + (1 \times SBP)] \div 3$. It is important to note that because this formula is based on the heart rate (specifically the left ventricular rate), it is dynamic. Most patients in critical care are attached to heart monitors and have arterial lines that measure and display heart rate and blood pressure, respectively, which allows MAP to be continuously displayed.

Figure 1: Key Components of Piloted Vasopressor Form (used as a communication tool)

Date:_____ Chart #:_____ Usual weight:_____ kg

Intensive care unit:

1. Which agent(s)?

☐ Norepinephrine ☐ Dopamine ☐ Vasopressin
☐ Epinephrine ☐ Phenylephrine ☐ Other: _____

2. Which indication?

☐ Septic shock ☐ Hypovolemic shock ☐ Unknown cause shock
☐ Cardiogenic shock ☐ Obstructive shock ☐ Other: _____

3. What is the target blood pressure and the tolerated range?

	Numerical value	*Tolerated range*				
☐ MAP (mmHg):	_____	MIN:	_____	MAX:	_____	N/A: _____
☐ SBP (mmHg):	_____	MIN:	_____	MAX:	_____	N/A: _____
☐ DBP (mmHg):	_____	MIN:	_____	MAX:	_____	N/A: _____

Target blood pressure rationale (optional): _____

_____

4. What is the threshold dose that should trigger physician reassessment? (see suggestions below)

(Maximum dose should be prescribed in mcg/min and calculated using patient's usual weight)

Norepinephrine or epinephrine ..... > 0.2 mcg/kg/min
Dopamine..... > 20 mcg/kg/min
Vasopressin ..... > 0.04 unit/min
Phenylephrine..... > 0.75 mcg/kg/min

Example of vasopressor prescription:

Norepinephrine 8 mg in 250 mL of NS for IV infusion to maintain MAP of 65 - 70 mmHg). Call MD if the dose reaches 0.2 mcg/kg/min.

Forty-eight clinicians (30 nurses, 8 residents, 4 intensivists, 6 pharmacists) piloted the form and assessed its usefulness. The perception that prescriptions for vasopressors were clear increased from 33% before implementation to 98% following implementation of the form during morning rounds. For 5 (17%) of the 29 consecutive patients requiring vasopressor therapy (duration ranging 1 to 5 days) for whom the form was used, it was found that the indication for vasopressor use changed over the course of treatment. Use of the form triggered reassessments and also facilitated communication about changes in indication and the required changes in vasopressor therapy to maximize cardiac output.

Recommendations

Important knowledge gaps exist regarding requirements for vasopressors for patients who are in shock, and the results of clinical research currently under way will be instrumental in guiding care.[7,8] This incident suggests that communication gaps exist among clinicians that may also need to be addressed concurrently with these studies. The following recommendations are suggested to improve communication:

- For written and electronic medication orders, specifying a target MAP or blood pressure range, in addition to the minimum value, can better communicate when vasopressor infusions should be reduced and will limit unnecessary exposure to these potent medications. Some evidence suggests that once vasopressor therapy has been instituted, measured blood pressure values tend to be higher than intended.[9]

- Frequent reassessment of vasopressor therapy by the multidisciplinary team is important to identify whether vasopressors are still required and to establish if a different agent is indicated (e.g., where the indication for a vasopressor has changed). Integrating reassessment into procedures and processes (for example, by using a form) may help to standardize practice.

- Opportunities exist to further empower members of the multidisciplinary team to identify and communicate concerns about the harmful effects of vasopressors. Earlier recognition of complications may improve patient outcomes. Implementing specific triggers, such as a defined vasopressor dose that warrants urgent communication with the most responsible physician, is one approach to consider. For example, patients whose condition deteriorates invariably become resistant to vasopressors; rapidly increasing doses of vasopressors could constitute a sensitive marker of deterioration. Therefore, careful monitoring of doses may help to identify another clinical reason for the worsening hypotension. This underlying cause (e.g., pulmonary embolism, hypovolemia, hemorrhage, myocardial infarction) can then be specifically targeted and treated.

Conclusion

Many healthcare practitioners play an instrumental role in the use of vasopressors. Improving patient care and safety requires a multidisciplinary approach, engaging nurses, physicians, and pharmacists. These recommendations focus on improving communication among team members, reassessing the indication for vasopressor therapy, and monitoring the dose.

Given that vasopressors constitute a mainstay of therapy for many types of patients experiencing hypotension, given their potency and systemic effect profile, and given that patients who receive vasopressors are among the most vulnerable patients in the healthcare system, there is opportunity to enhance patient safety through the learning that has been shared here and the recommendations presented.

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