vasopressors are agents that cause constriction of blood vessels, leading to an increase in blood pressure. Some vasopressors are also positive inotropes (capable of increasing contractility of the heart) and/or positive chronotropes (capable of increasing heart rate). Vasopressors are commonly administered intravenously in the critical care setting to treat conditions such as severe hypotension and cardiac arrest.

The hemodynamic effects of most vasopressors occur secondary to their interactions with receptors in the heart and vascular system. The receptors most relevant to the pharmacology of vasopressors are adrenoceptors. Adrenoceptors, sometimes referred to as adrenergic receptors, interact with norepinephrine, epinephrine, and chemically similar drugs (called adrenomimetic, adrenergic, or sympathomimetic agents). Adrenoceptors are classified as α- or β-adrenoceptors. The α-adrenoceptors are subdivided into α1- and α2-adrenoceptors, and β-adrenoceptors are subdivided into β1- and β2-adrenoceptors.1–3

The physiological response to adrenoceptor stimulation depends on the location of the receptors. A summary of adrenoceptor types, their primary locations, and the response when stimulated is provided in Table 1. The most significant adrenoceptors involved in the pharmacology of vasopressors are α1-, β1-, and β2-adrenoceptors. Vasocostriction of most blood vessels is mediated by α1-adrenoceptors. Some vasopressors also act as β-adrenoceptor agonists, which mediate inotropic, chronotropic, and vasodilatory effects.2 Therefore, the hemodynamic effects of vasopressors vary and can be quite complex. Table 2 summarizes the pharmacologic activity of vasopressors currently on the market.

Norepinephrine

Norepinephrine is one of the principal neurotransmitters (chemical substances involved in the transmission of nerve impulses) in the sympathetic nervous system and is released from nerve cells.3 Norepinephrine is indicated for the treatment of acute hypotension resulting from severe hypotension and cardiac arrest.
conditions such as spinal anesthesia, myocardial infarction, septicemia, blood transfusions, and drug reactions. This agent is also used adjunctively in the treatment of cardiac arrest and profound hypotension.

Norepinephrine is a potent α-adrenoceptor agonist and is therefore a strong vasoconstrictor, increasing systolic and diastolic blood pressures. In addition, norepinephrine stimulates β₁-adrenoceptors, so it increases both heart rate and contractility. Norepinephrine does not affect β₂-adrenoceptors. Therefore, vasodilation does not occur, vasoconstriction is unopposed, and reflex bradycardia can occur.

Epinephrine

Epinephrine is another neurotransmitter in the sympathetic nervous system, but it is not released from nerve cells; rather, epinephrine is a hormone secreted by the adrenal medulla. Epinephrine is used intravenously during advanced cardiac life support. It may also be used to treat other conditions, including anaphylactic shock and acute, severe asthma unresponsive to normal treatment.

Because epinephrine is a potent α- and β-adrenoceptor agonist, it is also a powerful vasoconstrictor, a positive inotrope, and a positive chronotrope. The effects of epinephrine are dose dependent. At lower doses (0.01 to 0.05 µg/kg per minute), β-adrenoceptor effects are predominantly observed. The β₁-adrenoceptor effects cause increased heart rate and force of contraction; the subsequent increase in cardiac output increases systolic blood pressure, but diastolic blood pressure may decrease as a result of vasodilation and increased blood flow through skeletal muscle beds resulting from β₂-adrenoceptor effects. The vasoconstrictive effects of epinephrine become more apparent as the dose is increased.

Dopamine

Dopamine, a precursor of norepinephrine and epinephrine, is also a neurotransmitter. This agent is found in both the central and peripheral nervous systems and is released from nerve cells. Dopamine is indicated in the treatment of shock due to myocardial infarction, trauma, endotoxic septicemia, open-heart surgery, renal failure, and chronic cardiac decompensation.

The effects of dopamine are complex and dose dependent. Dopamine directly stimulates dopaminergic receptors, α₁-adrenoceptors, and β₁-adrenoceptors, and it indirectly causes the release of endogenous norepinephrine. At low doses (1 to 2 µg/kg per minute), dopamine directly stimulates dopaminergic receptors on arteries in the kidneys, abdomen, heart, and brain and causes vasodilation. At these doses, urine output may increase, but blood pressure and heart rate are usually not affected. As the dose is increased (2 to 10 µg/kg per minute), dopamine stimulates β₁-adrenoceptors, resulting in positive inotropic and chronotropic effects—myocardial contractility and heart rate are increased, resulting in enhanced cardiac output. At higher doses (greater than 10 µg/kg per minute), dopamine exerts effects primarily on α₁ receptors, and extensive vasoconstriction causes blood pressure to increase. At doses greater than 20 µg/kg per minute, the effects of dopamine are similar to those of norepinephrine.

Phenylephrine

Phenylephrine is chemically related to epinephrine. Intravenous phenylephrine is used to treat hypotension resulting from shock, shocklike states, anesthesia, or hypersensitivity reactions to drugs.

Phenylephrine is a powerful vasoconstrictor that strongly stimulates α-adrenoceptors but has little effect on β-adrenoceptors of the heart. Its vasoconstrictive properties are similar to those of norepinephrine. Phenylephrine increases systolic and diastolic blood pressures in a dose-dependent manner, but because it has minimal effects on β receptors, heart rate and contractility are generally not affected. However, reflex bradycardia can accompany the use of phenylephrine.

Metaraminol

Metaraminol is indicated for the prevention and treatment of acute hypotension during spinal anesthesia and as an adjunct in the treatment of hypotension due to hemorrhage, drug reactions, surgical complications, and shock associated with brain damage from trauma or tumors.

Metaraminol causes vasoconstriction both directly as a result of

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Table 2 Vasopressors and receptor stimulation

<table>
<thead>
<tr>
<th>Vasopressor</th>
<th>Receptor(s) stimulated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>α₁, α₂, β₁</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>α₁, α₂, β₁, β₂</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Dopaminergic, α₁, β₁</td>
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<tr>
<td>Phenylephrine</td>
<td>α₁, α₂</td>
</tr>
<tr>
<td>Metaraminol</td>
<td>α₁, β₁, β₂</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>V₁, V₂</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>α₁, β₁, β₂</td>
</tr>
</tbody>
</table>

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its interaction with α-adrenoceptors and indirectly by causing the release of endogenous norepinephrine.21 Both systolic and diastolic blood pressures are increased. Metaraminol is generally considered a selective α1-adrenoceptor agonist,22,23 but it also stimulates β-adrenoceptors in the heart at low doses and has a positive inotropic effect, resulting in increased contractile force and cardiac output.24 Reflex bradycardia can result from vasoconstriction.25

**Ephedrine**

The primary use of intravenous ephedrine is to treat anesthesia-induced hypotension. It may also be used to treat hypotension resulting from sympathectomy or overdose of antihypertensive drugs.26

Ephedrine has direct and indirect α- and β-adrenoceptor activity; it affects α1-adrenoceptors primarily indirectly by causing the release of norepinephrine.1,17 Ephedrine causes an increase in systolic and diastolic blood pressures, cardiac contractility, and cardiac output.19,20 Heart rate can be increased, but generally it is not.18

**Vasopressin**

Vasopressin is a unique vasopressor for 2 reasons. First, its principal use is for a condition unrelated to its vasopressor properties. Vasopressin is an antidiuretic hormone indicated to inhibit diuresis in patients with diabetes insipidus.27 However, at higher doses, vasopressin causes vasoconstriction.22 Because there is a fair amount of evidence to support its effectiveness as a vasopressor, vasopressin is now considered as an alternative to epinephrine for the treatment of adult shock-refractory ventricular fibrillation during advanced cardiac life support.6

Vasopressin is a distinctive vasopressor also because its vasoconstrictive effects do not result from its interaction with adrenoceptors; rather, vasoconstriction arises from vasopressin’s actions on vasopressin receptors. Vasopressin receptors are classified as V-1 and V-2 receptors. V-1 receptors are located on arterial smooth muscle, and V-2 receptors are found in renal tubules. Vasopressin’s interaction with V-1 receptors is responsible for its potent vasopressor effects.28

**Dobutamine**

Dobutamine is indicated for short-term inotropic support in patients with cardiac decompensation due to depressed contractility resulting either from organic heart disease or from cardiac surgery.24

Classifying the drugs that have been discussed so far as vaspressors has been fairly straightforward. However, including dobutamine in this class of drugs is more difficult. Although dobutamine is undoubtedly an inotrope, some authors consider it a vasopressor,25,26 whereas others consider it a vasodilator.28 The reason for this disparity is because the pharmacology of dopamine is quite complex.

Dobutamine is a racemic mixture of 2 isomers. One isomer is a strong α1-adrenoceptor agonist and can act as a vasopressor, whereas the other isomer is an α1-adrenoceptor antagonist.27 One isomer’s α1-adrenoceptor properties may cancel out the effects of the other isomer,28 but this may not always be the case; both iso-mers are β-adrenoceptor agonists.17

Dobutamine is generally considered a relatively selective β1-adrenoceptor agonist because the net effect of dobutamine administration is an increase in cardiac contractility.29 As a consequence of the increased cardiac output, there can be a reflex decrease in vascular tone and vasodilation may result.1 However, because dobutamine can have modest effects on α1-adrenoceptors in blood vessels, vasoconstriction may occur and cause blood pressure to increase significantly in some patients.17 Dobutamine increases heart rate, but the chronotropic effects are observed only at higher doses.5

**Conclusion**

The hemodynamic effects of vasopressors vary from drug to drug, but may also vary in a dose-dependent manner in a single agent. This variation results from differing pharmacological actions on receptors (Table 2). Careful and frequent monitoring of hemodynamic parameters, including blood pressure, pulse, and other measures as required, is crucial to ensure optimal outcomes with the use of vasopressors.

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**References**


Hemodynamic Pharmacology of Intravenous Vasopressors
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