HYPOTENSIVE AND HYPERTENSIVE AGENTS: MECHANISMS, DOSE–RESPONSE RELATIONSHIPS, CLINICAL USE, ADVERSE EFFECTS, AND SAFETY PRINCIPLES

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Abstract. Arterial blood pressure is determined by cardiac output and peripheral vascular resistance; these parameters are finely regulated through the renin–angiotensin–aldosterone system, the sympathetic nervous system, renal sodium–water handling, and endothelial mediators. For this reason, the pharmacology of hypotensive (blood-pressure–lowering) and hypertensive (blood-pressure–raising, pressor) agents cannot be reduced to the simple idea of “lowering or raising the number”: such agents influence the heart, kidneys, brain, and peripheral vessels through different pathways and serve distinct goals in acute and chronic clinical settings. In this IMRAD-format article, the main classes of hypotensive drugs (diuretics, ACE inhibitors, angiotensin receptor blockers, calcium channel blockers, beta-blockers, central alpha2-agonists, peripheral vasodilators, and others) and hypertensive agents (norepinephrine, epinephrine, phenylephrine, vasopressin, dobutamine, and related vasopressor/inotropic drugs) are systematically analyzed with respect to mechanisms, dose–response patterns, clinical applications, adverse effects, and safety-management principles. In the Results section, comparative tables across drug classes are provided, highlighting key decision criteria such as comorbidity profile, target-organ damage, age, pregnancy, drug–drug interactions, and monitoring requirements. The Discussion integrates contemporary recommendations (WHO 2021; ISH 2020; ESH 2023; ESC 2024) and argues for a strategy of evidence-based selection combined with optimized monitoring, placing the individual risk profile at the center of therapeutic choice. This paper is intended for educational and scientific use; practical treatment decisions must be made by a physician in accordance with clinical indications and local protocols.

Keywords: arterial hypertension, hypotensive agents, vasopressors, inotropic drugs, RAAS, beta-blocker, ACE inhibitor, ARB, calcium channel blocker, safety and monitoring

Introduction

Arterial blood pressure is one of the key hemodynamic indicators that ensures the organism's perfusion needs and can be expressed by the classical relationship: Blood pressure ≈ Cardiac output × Total peripheral resistance. Cardiac output depends on heart rate, stroke volume, venous return, and myocardial contractility, while peripheral resistance is shaped by arteriolar tone, endothelial function, and metabolic as well as neurohumoral mediators. The kidneys regulate circulating volume via sodium and water balance, whereas the renin–angiotensin–aldosterone system controls both vascular tone and fluid retention. The sympathetic nervous system provides rapid control through alpha and beta adrenergic receptors, and the endothelium modulates micro- and macro-hemodynamics through the balance of nitric oxide, prostacyclin, endothelin, and related mediators.

Because of this complex regulation, two opposite yet complementary drug groups are clinically crucial: hypotensive and hypertensive agents. The former are primarily used to achieve target blood-pressure ranges in conditions such as arterial hypertension, heart failure, nephropathy, and high atherothrombotic risk. The latter are used to restore perfusion in acute hypotension, shock, severe sepsis, anaphylaxis, or perioperative hemodynamic instability. Importantly, "lowering blood pressure" is not always beneficial: for example, during certain phases of acute ischemic stroke or in severe aortic stenosis, excessive hypotension can worsen tissue perfusion. Likewise, "raising blood pressure" is not only about increasing a number; it should be judged by improved tissue perfusion, faster lactate clearance, and reduction of organ dysfunction.

Dose–response relationships are central to pharmacology. A single drug may selectively activate or inhibit specific receptors at lower exposures, while at higher exposures additional receptor populations and secondary pathways may be engaged. In adrenergic agonists, for instance, alpha1-mediated vasoconstriction, beta1-mediated inotropy, and beta2-mediated bronchodilation/vasodilation can manifest differently depending on exposure level, receptor density, and tissue perfusion. A similar logic applies to hypotensive classes: diuretics lower blood pressure by increasing sodium excretion, but compensatory activation of RAAS and sympathetic tone may follow; ACE inhibitors or ARBs can blunt this compensation and thereby enhance cardio- and nephroprotective effects.

Modern recommendations have moved away from a “one universal drug” approach and prioritize risk stratification and combination therapy (often as single-pill combinations) to achieve earlier and more stable control. In acute shock, vasopressor selection is adapted to shock etiology, cardiac function, arrhythmia risk, and the state of microcirculation; in sepsis, norepinephrine is recommended as a first-line agent. The purpose of this article is to present hypotensive and hypertensive agents systematically by mechanism, dose–response behavior, clinical use, adverse effects, and monitoring demands, and to explain practical selection criteria through comparative tables and analysis.

Materials and Methods:A narrative–analytical review approach was used. Materials were compiled from international clinical guidelines on the pharmacological management of hypertension and shock, as well as core sources in pharmacology. For hypotensive therapy, WHO (2021) guidance for the pharmacological treatment of hypertension, ISH (2020) global practice guidelines, ESH (2023) recommendations for arterial hypertension, and updated ESC (2024) guidance served as the conceptual framework. For hypertensive (pressor) therapy, vasopressor selection and the sepsis approach were aligned with Surviving Sepsis Campaign (2021) recommendations.

Drug classes were structured using the following criteria: (1) primary receptor or enzyme target and mechanism, (2) clinical indications and priority use-cases, (3) dose–response and pharmacodynamic characteristics (selectivity, onset, duration, tolerance), (4) adverse effects and major contraindications, and (5) monitoring requirements (ECG, electrolytes, renal function, and perfusion markers). Quantitative dosing parameters are not provided because dosing must be individualized according to age, body size, comorbidity profile, and local protocols; therefore the information is educational in nature. The Results section summarizes findings through comparative tables, and the Discussion integrates decision-making algorithms, combination-therapy rationale, and safety-management principles.

Results

1) Hypotensive agents: major classes and mechanisms. From a practical perspective, hypotensive drugs can be grouped into two broad directions: (a) agents that manage volume and sodium balance (diuretics, mineralocorticoid receptor antagonists), and (b) agents that modulate vascular tone and neurohumoral activity (ACE inhibitors, ARBs, calcium channel blockers, beta-blockers, alpha1-blockers, central alpha2-agonists, and direct vasodilators). Choosing a drug is not only about the magnitude of blood-pressure reduction but also about target-organ protection

(nephroprotection, cardio-/cerebroprotection), metabolic neutrality, and patient adherence.

2) Hypertensive agents: the role of vasopressors and inotropes. Hypertensive agents are most commonly used in critical-care settings. Their goal is to restore mean arterial pressure and tissue perfusion. Adrenergic agonists can combine alpha1-mediated vasoconstriction, beta1-mediated enhancement of myocardial contractility, and beta2-mediated vasodilation/bronchodilation. Vasopressin increases vascular tone through V1 receptors and can be useful as an adjunct to catecholamines in selected types of shock. In sepsis, norepinephrine is recommended as a first-line vasopressor because it provides strong alpha1 activity with a relatively controllable beta1 component.

3) Dose–response and clinical balance. For hypotensive drugs, increasing exposure may raise the probability of symptomatic hypotension, electrolyte disturbances, bradycardia, or reflex tachycardia; therefore titration and monitoring are essential. For vasopressors, higher exposure increases the risk of peripheral ischemia, arrhythmias, myocardial ischemia, and reduced splanchnic perfusion. Consequently, pressor therapy is evaluated by “target pressure + clinical perfusion” criteria, including urine output, mental status, skin perfusion, capillary refill time, and lactate dynamics.The tables below compare hypotensive and hypertensive drug classes from the viewpoints of mechanism, clinical use, and safety.

Table 1. Hypotensive drug classes: mechanism, clinical advantages, and safety considerations.

Class	**Primary target/mechanism**	**Clinical advantages**	**Key risks and cautions**	**Monitoring focus**
Diuretics (thiazide/thiazide-like)	Reduce sodium reabsorption; decrease volume and peripheral resistance	Widely used; effective in combinations; associated with reduced stroke risk	Electrolyte disturbances (K, Na), metabolic effects; may worsen gout	Electrolytes, glucose/lipid profile, BP and symptoms

ACE inhibitors	Decrease angiotensin II formation; increase bradykinin; vasodilation and nephroprotection	Useful in diabetic nephropathy, heart failure, post-MI states	Cough, angioedema; hyperkalemia; contraindicated in pregnancy	Creatinine/ eGFR, K+, BP, cough/reactions
ARBs (AT1 blockers)	Block AT1 receptor; suppress RAAS effects	Alternative when ACE inhibitors are not tolerated; cardio-/nephroprotection	Hyperkalemia; risk of reduced renal perfusion; contraindicated in pregnancy	Creatinine/ eGFR, K+, BP
Calcium channel blockers (DHP / non-DHP)	Block L-type Ca2+ channels: DHP mainly vascular; non-DHP affects heart/AV conduction	Angina; some arrhythmias (non-DHP); effective in older adults	Peripheral edema, flushing; non-DHP: bradycardia/AV block risk	Heart rate, ECG when needed, edema, BP
Beta-blockers	Beta1 blockade reduces cardiac output and renin release	Beneficial in IHD, arrhythmias, post-MI, selected HF phenotypes	Bradycardia, bronchospasm (non-selective), masked hypoglycemia	Pulse, ECG, bronchial symptoms, glucose in diabetes
Central alpha2-agonists	Reduce central sympathetic outflow	Option in selected resistant cases; some	Sedation, dry mouth; rebound hypertension	Drowsiness, BP, HR; adherence/continuity of use

		agents used under protocol in pregnancy	after abrupt withdrawal	
Peripheral vasodilators	Direct arteriolar vasodilation	Add-on in resistant hypertension; useful in selected settings	Reflex tachycardia, fluid retention; headache	Pulse, edema, BP; need for combination

Table 2. Hypertensive (pressor) agents: receptors, hemodynamic effects, and key risks.

Agent (pressor)	**Receptor/ pathway**	**Main hemodynamic effect**	**General clinical context**	**Key risks**
Norepinephrine	α1 > β1	Strong vasoconstriction with moderate inotropy; increases MAP	Recommended first-line in septic (vasodilatory) shock	Peripheral ischemia, arrhythmias; extravasation risk
Epinephrine	β1/β2 and α1 (dose-dependent)	Inotropy + bronchodilation; vasoconstriction at higher exposures	Protocolized use in anaphylaxis and selected resuscitation settings	Tachyarrhythmia, increased lactate, myocardial ischemia
Phenylephrine	Selective α1	Vasoconstriction; reflex bradycardia may occur	Considered when tachyarrhythmia risk is high	Reduced perfusion, bradycardia, peripheral ischemia

Vasopressin	V1 (vascular) / V2 (renal)	Adjunct vasoconstriction; supports MAP	Adjunct to norepinephrine in septic shock in some protocols	Ischemic complications, hyponatremia; context-sensitive effects
Dobutamine (inotrope)	β1 > β2	Increases contractility and cardiac output	Low cardiac output/cardiogenic component in shock	Tachyarrhythmia, hypotension (β2), increased oxygen demand
Dopamine (historical use)	Dose-dependent: dopaminergic/β/α effects	Variable mix of inotropy and vasoconstriction	Limited role in some protocols; caution due to arrhythmia risk	Arrhythmias, variable response, endocrine effects

Table 3. Quick clinical map: choosing hypotensive vs pressor strategies by scenario.

Clinical situation	**Primary goal**	**More suitable approach (general)**	**What must be monitored**
Chronic arterial hypertension	Reduce long-term risk and protect target organs	First-line classes + combination therapy with lifestyle measures	Home/ambulatory BP, renal function, electrolytes, adherence
Hypertensive crisis (acute)	Safe reduction while	Stepwise reduction per	Neurologic status, ECG, renal indices,

	maintaining organ perfusion	protocol; assess cause and organ injury	symptomatic hypotension
Sepsis or vasodilatory shock	Restore MAP and improve microcirculation	Fluids + norepinephrine first-line; add agents if needed	Lactate trends, urine output, skin perfusion, arrhythmias
Cardiogenic shock	Increase cardiac output and maintain perfusion	Etiologic treatment + evaluate need for inotropic support	ECG, cardiac biomarkers, urine output, pulmonary congestion, arrhythmias

Discussion

The systematization presented in this paper supports a core principle of clinical practice: selecting drugs that influence blood pressure is not merely about normalizing a number, but about building a strategy aligned with the patient's overall risk profile. In chronic arterial hypertension, first-line classes typically include thiazide or thiazide-like diuretics, ACE inhibitors or ARBs, and calcium channel blockers; for many patients, combination therapy is recommended to achieve faster control and improved adherence. Beta-blockers can be especially useful in specific contexts such as ischemic heart disease, arrhythmias, heart failure, or thyrotoxicosis.

Conversely, in acute hypotension and shock, vasopressor/inotrope selection should begin with an etiologic diagnosis. Because peripheral vasodilation and relative hypovolemia often dominate in sepsis, norepinephrine—characterized by strong alpha-adrenergic vasoconstriction—is frequently an optimal choice. In cardiogenic shock, reduced contractility may be the leading problem, increasing the need for an inotropic component; however, clinicians must always consider the risks of arrhythmia and increased myocardial oxygen demand. In anaphylaxis, the broad alpha/beta profile of epinephrine is life-saving, but its use should remain within protocolized medical supervision.Universal elements of safety management exist across these drug categories. In hypotensive therapy, it is crucial to monitor renal function and electrolytes, assess orthostatic hypotension risk, and account for drug–drug interactions in polypharmacy. For ACE inhibitors/ARBs, potassium elevation and creatinine dynamics are particularly important; for diuretics, sodium/potassium shifts and effects on glucose–lipid metabolism must be considered. Central alpha2-agonists may be

limited by sedation and rebound hypertension after abrupt discontinuation, while alpha1-blockers are constrained by orthostatic hypotension.

In vasopressor therapy, continuous ECG monitoring, invasive or close hemodynamic surveillance, clinical markers of tissue perfusion, signs of peripheral ischemia, and infusion-line safety are priorities. Target pressure selection should be individualized: in patients with long-standing hypertension, autoregulatory thresholds for perfusion may be higher, but excessive vasoconstriction can still impair microcirculation. Therefore, pressors must be considered together with fluid resuscitation, etiologic treatment, and organ-support strategies.From an educational standpoint, placing hypotensive and hypertensive agents within a unified comparison framework strengthens clinical reasoning: whichever pathophysiological component dominates, therapy should target that key “link.” Nonetheless, protocol adherence, patient safety, and physician oversight remain irreplaceable.

Conclusion

Hypotensive and hypertensive agents are two-sided yet complementary instruments for hemodynamic control. Hypotensive drugs play a central role in reducing target-organ damage and long-term cardiovascular risk in arterial hypertension, and class selection should be tailored to comorbidity profile, organ protection, and adherence. Hypertensive (pressor) agents are used to restore perfusion in acute hypotension and shock; because of dose–response behavior and adverse-effect risks, they must be applied in conjunction with protocols, monitoring, and etiologic therapy. Overall, effective and safe pharmacotherapy is best achieved through the triad of an appropriate drug class, individualized selection, and systematic monitoring.

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