PHYSIOLOGY AND PHARMACOLOGY OF VASOACTIVE DRUGS: THE IMPACT ON THE CARDIOVASCULAR SYSTEM OF CRITICALLY ILL PATIENTS

Geovanna Araújo Maciel[1], Isabel Cristina Araújo Vieira[2], Thiago dos Santos Silva[3], Maria Luiza Moura Sousa Silva[4], Daiane Furtado Maluf[5], Janaína Gonçalves de Souza[6], Arlete Angelim de Santana Novais[7], Ian Santana Diotildes[8], Áurea Vitória by Leandro Buso[9] and Priscila Tatiane Luchi da Silva[10]

ABSTRACT

The text addresses the importance of vasoactive drugs in the management of patients with hemodynamic instability, detailing their effects on blood pressure, vascular tone, and cardiac output. The classifications of these drugs, the clinical indications, the need for adequate monitoring, and the risks associated with their use are explored. The research, of a bibliographic nature, seeks to offer an in-depth understanding of the physiology of blood vessels and the pharmacology of vasoactive drugs, especially in intensive care settings.

Keywords: Vasoactive drugs, Hemodynamic monitoring.

INTRODUCTION

Vasoactive drugs are groups of high-potency medications, essential for the management of patients in hemodynamic instability. Its role is to regulate vascular tone and blood pressure, which is essential to maintain adequate organ perfusion. These substances can be classified into 3 groups according to their effects, such as vasoconstriction, vasodilation and inotropism. These effects are played by the sensitivity and quantity of receptors in different places, such as in the heart and blood vessels (CRUZ, et al. 2021).

These substances can be used to increase or decrease vascular tone, directly influencing blood pressure, cardiac output, and peripheral vascular resistance. As well as the increase in heart rate through increased contractility, by the positive inotropism caused

[1] Afya – Faculties of Medical Sciences of Itabuna- Bahia
[2] Mato Grosso State University - Mato Grosso
[3] Afya – Faculties of Medical Sciences of Itabuna- Bahia
[4] Uninovafapi University Center - Piauí
[5] Afya – Faculties of Medical Sciences of Itabuna- Bahia
[6] Universidade Brasil – São Paulo
[7] Estácio de Sá University - Vista Carioca - Rio de Janeiro
[8] Estácio College – IDOMED - Bahia
[9] Afya – Faculties of Medical Sciences of Palmas - Tocantins
[10] Universidade Brasil – São Paulo

as an effect of these medications. Understanding the physiology of blood vessels and the pharmacological action of these drugs is essential for their safe and effective application in clinical practice, for the proper management of patients in a critical hemodynamic state (DE OLIVEIRA, et al. 2023).

Although they are drugs with excellent therapeutic effects, it is important to highlight the importance of carrying out other measures before these medications, such as oxygenation and adequate volume replacement. During the use of vasoactive drugs, it is important to carry out adequate hemodynamic monitoring, preferably invasive, to assess such changes and adjust their doses more appropriately (SANTOS, et al. 2022).

The most commonly used vasoactive drugs in intensive care are sympathomimetic amines, also known as catecholamines, non-digitalis cardiotonics, and arteriovenous vasodilators (ARRUDA, et al. 2024).

It is worth noting that although the effects of vasoactive drugs are fast-acting, they are also short-acting, and their response is dose-dependent. For this reason, they should preferably be administered in an infusion pump in an in-hospital environment. The receptors responsible for these effects are α1, α2, β1, β2 and V1. Aiming to increase or decrease blood pressure to allow better coronary and cerebral perfusion (CRUZ, et al. 2021).

The main catecholamines used in medical practice are norepinephrine, dopamine adrenaline, dobutamine and isoproterenol. The main non-digitalis cardiotonics are anrinone, milrinone, dopexamina, ibopamine, and levosimendan. And the most commonly used vasodilators are sodium Nitroprusside known as nipridi and nitroglycerin known as tridiu (DA COSTA, et al. 2022).

Mastery in the application of these drugs requires a deep understanding of cardiac physiology and vascular endothelium, as well as pharmacokinetics and pharmacodynamics of these medications. These are essential factors for therapeutic success in an intensive care setting (CAVALCANTE, et al. 2024).

OBJECTIVE

The general objective of this study is to cite and present a detailed analysis of the physiology of blood vessels and the pharmacology of vasoactive drugs, highlighting how these substances influence the cardiovascular disease. It is intended to provide an in-depth understanding of the functioning and clinical application of these drugs in situations that require hemodynamic interventions.

SPECIFIC OBJECTIVES

1. Determine Vasoactive Drug Classifications
2. Understand what are the main Clinical Indications for each Vasoactive Drug
3. Cite how proper monitoring is done
4. Establish the Risks and Adverse Effects
5. Stipulate the appropriate form of De-escalation of Drugs

METHODOLOGY

Considering that theoretical studies are an indispensable basis for field and laboratory research, we opted for conceptual deepening and search for official data on the object of study, allowing the knowledge of reality as well as the possibility of critical reflection on the subject within the scope of the Brazilian reality.

Based on the understanding of Creswell (2007) for whom the Literature Review is configured as a preliminary stage of scientific studies, then the research is a Literature Review in which articles published in the National Library of Medicine (Pubmed), Virtual Health Library (VHL), Web of Science, Lilacs and Capes Journals were used as the basis of the study by descriptors obtained by the Health Sciences Descriptors (DeCS) of the VHL.

This is a literature review of articles published in the National Library of Medicine (Pubmed), Virtual Health Library (VHL), Web of Science, Lilacs and Capes Journals by descriptors obtained by the Health Sciences Descriptors (DeCS) of the VHL. The following descriptors were searched: Vasoactive drugs AND Cardiovascular system AND pharmacology AND Physiology in "All fields".

For the selection of articles, the following steps were followed: (I) search for articles in the databases; (II) reading of titles and abstracts, with analysis according to the eligibility criteria and; (III) full-text analysis of the papers, including in the systematic review only those required by the inclusion criteria and did not meet any of the exclusion criteria.

Published studies were eligible if they met the following criteria: (1) studies involving the physiology and mechanism of action of vasoactive drugs; 2) studies that had the object of study the relationship between vasoactive drugs and critically ill patients; (3) articles that studied classification, indications, risks, and adverse effects of vasoactive drugs; (4) articles published in the last 4 years. There were no restrictions on sample size or foreign language.

As exclusion criteria, articles were excluded that: (1) were published before 2020; (2) studied situations that do not include the use of vasoactive drugs; (3) duplicates; (4) had no direct relationship with the use of vasoactive drugs, their mechanisms of action, adverse effects, and de-escalation.

DEVELOPMENT

The cardiovascular system aims to perfuse tissues. Blood vessels are responsible for transporting blood through the body, regulating flow according to the metabolic needs of the tissues, carrying nutrients, glucose and O2. These vessels are formed by three main layers: intima (inner layer), media (composed of smooth muscle) and adventitia (outer layer). Through smooth muscle, it is possible to perform contraction and relaxation on the walls of the vessels. And these mechanisms are regulated by a series of stimuli, including the autonomic nervous system, circulating hormones, and local mediators such as nitric oxide and endothelin (MOURA, et al. 2024).

Vascular tone is determined by the balance between the vasoconstrictor systems, which is stimulated by the presence of catecholamines such as noradrenaline, adrenaline, dobutamine, and dopamine. And the vasodilation process is mediated by factors such as nitric oxide, through sodium nitroprusside and nitroglycerin. Precise regulation of this tone is essential to maintain blood pressure and tissue perfusion, especially in situations of hemodynamic instability (MORAIS, et al. 2020).

Among vasoactive drugs, it is also possible to identify cardiotonic drugs with a positive inotropic effect, increasing cardiac contractility as a mechanism of action, mainly through the b1 receptor. In this drug group, Milrinone, Anrinone, and levosimendan stand out (CRUZ, et al. 2021).

Catecholamines work by stimulating adrenergic receptors (mainly alpha-1) on vessel walls, resulting in increased peripheral vascular resistance and blood pressure. They are often used in septic or cardiogenic shock conditions, where there is a need to restore blood pressure. The receptors used to perform by catecholamines are α1, α2, β1, β2 and V1 (AGOSTINHO, et al. 2024).

Each receptor plays a greater sensitivity to some therapeutic effects. The α1 receptor is present in the blood vessel and is responsible for generating vasoconstriction of arteries and veins, through smooth muscle contraction, thus causing an increase in peripheral vascular resistance, enabling an increase in preload and improving cardiac output (GUERRA, et al. 2024).

The α2 receptor is present in the blood vessel and does not exert many hemodynamic effects, and can inhibit the release of insulin and norepinephrine. The β1 receptor is present in the heart and performs one of the main functions of increasing the heart rate and increasing the force of myocardial contraction. The β2 receptor, on the other hand, is present in the blood vessels and lungs and has the function of causing vasodilation, thus causing a decrease in peripheral vascular resistance, thus decreasing

preload. The β2 receptor has an important role in causing bronchodilation in patients with asthma attacks. And V1 receptors are present in the vascular endothelium and are stimulated by vasopressin, causing peripheral vasoconstriction (FONTANELE, et al. 2024).

Norepinephrine is an endogenous catecholamine that performs the function of primary agonist of alpha and beta adrenergic receptors. It is a metabolic derivative of dopamine, being released endogenously in response to stress stimuli. Administration exogenously at a dose of 0.01 to 3.0 mcg/kg/min. Its main indication is in distributive shocks such as septic shock, but it is also indicated in cardiogenic and hypovolemic shocks. It acts on α1 and β1 receptors, that is, it has a vasoconstriction and inotropism effect (CAVALCANTE, et al. 2024).

Adrenaline is also part of the endogenous catecholamines, it is a primary agonist drug of the α1, β1 and β2 adrenergic receptors. Its administration exogenously should occur in doses of 1 to 10 mcg/min. It is the drug of choice in anaphylactic shock or asthma attack. It is the second-line drug of septic shock. Its side effect is an increase in lactate and myocardial oxygen demand, and increases the risk of arrhythmias (DE OLIVEIRA, et al. 2023).

Dobutamine is a drug that has an important inotropic effect, and is the drug of choice in myocardial dysfunction, it is a fast-acting drug, with a pharmacological half-life of approximately 2 minutes. Its action is performed through β1 and β2 receptors, thus having an inotropic effect and peripheral vasodilation. It is used in doses between 2.5 to 20 mcg/kg/min. Dobutamine and dopamine in intermediate doses have both positive inotropic effects and vasoactive properties, which makes them useful in situations of low cardiac output associated with hypotension (GUERRA, et al. 2024).

Vasopressin is an antidiuretic hormone, with a vasoconstrictor effect on the V1 receptor, and is indicated for use in refractory shocks with the use of noradrenaline. And as a side effect it can cause rebound hypotension (DE SOUZA, et al. 2021).

On the other hand, vasodilators, such as sodium nitroprusside, potent arterial and venous vasodilator and nitroglycerin, are only intravenous vasodilators. Vasodilators in general work by relaxing the smooth muscle of the vessels, reducing peripheral vascular resistance and promoting a decrease in blood pressure. These drugs are useful in conditions such as heart failure and hypertensive crises, where it is necessary to reduce afterload to improve cardiac output (FAUSTINO, et al. 2020).

Sodium nitroprusside causes arterial and venous peripheral vasodilation by direct action of its metabolite nitric oxide on the smooth muscle of the endothelium. It also causes an increase in cardiac output and as adverse effects we can highlight cyanide poisoning,

hypotension, headache, disorientation, nausea and palpitation. Its therapeutic dose is between 0.5 and 5 mcg/kg/min (GONÇALVES, et al. 2021).

Inotropes are non-digitalis cardiotonic drugs, their effect is to increase myocardial contractility, thus increasing the heart rate. They are a group of drugs that have different mechanisms of action. Among its indications is decompensated heart failure and heart failure after AMI. They are represented by milrinone and levosimendan (DE OLIVEIRA, et al. 2023).

Milrinone is a phosphodiesterase III inhibitor drug that increases contractility and chronotropism by increasing the concentration of intracellular cyclic AMP, and promotes pulmonary arterial vasodilation. With the increase in contractility and conduction velocity in the myocardial stimulus, the expected effect is an increase in cardiac output, but it does not increase the consumption of O2 by the myocardium. Its main indication is in severe decompensated HF, and it can be used in patients who are chronic beta-blockers. Its therapeutic doses are slow bolus infusion 50 µg/kg in 10 minutes and its maintenance 0.375 to 0.750 µg/kg/min (DA SILVA, et al. 2021).

Levosimendan is a drug that has a positive inotropic effect, its mechanism of action is through an increase in myocardial sensitivity to calcium, thus increasing the affinity and amount of calcium released from the sarcomere to the actin-myosin complex. And just as milrinone does not increase the consumption of O2 by the myocardium and can also be used in patients with chronic use of beta-blockers. Its main indications are represented by decompensated HF, LV failure after AMI, and myocardial dysfunction after cardiopulmonary bypass. Its therapeutic doses in loading dose are 12 µg/kg in 10 minutes and its maintenance is 0.1 to 0.4 µg/kg/min (PANSANI, et al. 2024).

The use of vasoactive drugs requires a deep understanding of their pharmacokinetics and pharmacodynamics, as well as close patient monitoring. Dose adjustment should be made based on clinical response, as inappropriate use may result in complications such as tissue ischemia or organ dysfunction. For example, overuse of vasoconstrictors can lead to severe vasoconstriction, decreasing blood flow to vital organs (CRUZ, et al. 2021).

FINAL CONSIDERATIONS

Understanding the physiology of blood vessels and the pharmacology of vasoactive drugs is essential for the proper management of patients in critical hemodynamic status. Vasoactive drugs are powerful tools that, when used correctly, can save lives by restoring tissue perfusion and stabilizing the patient's hemodynamics (FREIRE, et al. 2024).

However, its use requires a careful approach, and it should be used with the appropriate doses and indications, always considering its form of application, its potential risks associated with excessive doses or the inappropriate choice of drug for the clinical picture, and performing adequate patient monitoring. Thus, a solid knowledge about the mechanisms of action of these drugs is indispensable for health professionals working in areas such as intensive care and cardiology (RANGEL, et al. 2023).

REFERENCES

1. AGOSTINHO, Clarice Terranova et al. Utilização de Drogas Vasoativas em Unidades de Terapia Intensiva: Uma Revisão Farmacocinética e Farmacodinâmica. Revista CPAQV-Centro de Pesquisas Avançadas em Qualidade de Vida, v. 16, n. 2, 2024.

2. ARRUDA, Bianca Fernandes Távora et al. Uso de digoxina em paciente com difícil desmame de dobutamina: um relato de caso. Arq. bras. cardiol, p. 227-227, 2024.

3. CAVALCANTE, Michelly Rodrigues et al. Perfil Epidemiológico dos Pacientes com Insuficiência Cardíaca em Hospital Público do Distrito Federal. Revista Contemporânea, v. 4, n. 7, p. e4938-e4938, 2024.

4. CRUZ, Rafaela da Silva et al. Utilização de drogas vasoativas em uma unidade de cuidados intensivos cardiológica: coorte retrospectiva. Clinical and biomedical research. Porto Alegre, 2021.

5. DA COSTA JUNIOR, Valmir Alves et al. Uso de drogas vasoativas no manejo do choque: uma revisão da literatura. Research, Society and Development, v. 11, n. 10, p. e149111032453-e149111032453, 2022.

6. DA SILVA, Maria da Conceição Rodrigues; JÚNIOR, Francisco Alves Lima; LEITE, Cristina Limeira. O Atendimento Humanizado na Sala Vermelha da Emergência de um Hospital Público no Municipio de Imperatriz do Maranhão: Relato de experiência. Revista Extensão, v. 5, n. 2, p. 61-68, 2021.

7. DE OLIVEIRA, Caio Bismarck Silva et al. Cuidados de enfermagem na administração de drogas vasoativas em Unidade de Terapia Intensiva: uma revisão integrativa. Revista Cereus, v. 15, n. 4, p. 268-282, 2023.

8. DE SOUZA, Leandro Aparecido; CONSORTI, Ane Helise; MACHADO, Nadyne Leite Martins. Cuidados de enfermagem na administração de drogas vasoativas em pacientes internados na unidade de terapia intensiva. Medicus, v. 3, n. 2, p. 22-28, 2021.

9. FAUSTINO, Tássia Nery. Drogas vasoativas e principais dispositivos invasivos utilizados no paciente crítico. 2020.

10. FONTENELE, Esther Sampaio et al. Correlação Clínica e Farmacológica no uso de Drogas Vasoativas para o Tratamento do Choque. Revista Foco, v. 17, n. 4, p. e4819-e4819, 2024.

11. FREIRE, Rodrigo Dias et al. Mobilização Precoce durante o Uso de Drogas Vasoativas em Pacientes Críticos: Revisão Integrativa. ID on line. Revista de psicologia, v. 18, n. 71, p. 171-181, 2024.

12. GONÇALVES, Allana Dupont et al. Perfil dos pacientes atendidos no primeiro ano de funcionamento de uma unidade de terapia intensiva: um estudo retrospectivo. Revista de Administração em Saúde, v. 21, n. 82, 2021.

13. GUERRA, Denise Krishna Holanda et al. Impacto das Drogas Vasoativas na Recuperação de Pacientes com Choque Cardiogênico: Evidências Recentes. Brazilian Journal of Implantology and Health Sciences, v. 6, n. 8, p. 3343-3367, 2024.

14. GUERRA, Denise Krishna Holanda et al. Impacto da dobutamina na estabilização hemodinâmica de pacientes em insuficiência cardíaca descompensada. Journal of Medical and Biosciences Research, v. 1, n. 4, p. 67-80, 2024.

15. MOURA, Guilherme Rodrigues Fontes; MOREIRA, Thaís Fernanda Faria. O uso de drogas vasoativas no tratamento do choque séptico. 2024.

16. MORAIS, Amanda Mariano et al. Exercício como mobilização precoce em pacientes com uso de drogas vasoativas. Revista Brasileira de Fisiologia do exercício, v. 19, n. 4, p. 301-311, 2020.

17. PANSANI, Victor Gasques et al. Terapia inotrópica em pacientes com insuficiência cardíaca crônica avançada. Revista Eletrônica Acervo Médico, v. 24, p. e15039-e15039, 2024.

18. RANGEL, Larissa; DA SILVA, Adilson Marques. Drogas vasoativas e cuidados de enfermagem. Revista Remecs-Revista Multidisciplinar de Estudos Científicos em Saúde, p. 46-46, 2023.

19. SANTOS, Thiago Tavares dos et al. Suporte hemodinâmico no choque e uso de drogas vasoativas. 2022.