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CARDIOVASCULAR RISKS ASSOCIATED WITH THE SYSTEMIC USE OF NAPHAZOLINE: AN INTEGRATIVE REVIEW

RISCOS CARDIOVASCULARES ASSOCIADOS AO USO SISTÊMICO DE NAFAZOLINA: UMA REVISÃO INTEGRATIVA

RIESGOS CARDIOVASCULARES ASOCIADOS AL USO SISTÉMICO DE NAFAZOLINA: UNA REVISIÓN INTEGRADORA

https://doi.org/10.56238/sevened2025.037-041

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ABSTRACT

Naphazoline, an alpha-adrenergic sympathomimetic amine widely used in nasal decongestants and ophthalmic solutions, has systemic absorption potential that may lead to adverse cardiovascular effects. This integrative review aimed to critically analyze scientific evidence published between 2015 and 2025 regarding the cardiovascular risks associated with the systemic or abusive use of naphazoline. The search was conducted between November and December 2025 in the PubMed/MEDLINE, SciELO, and Scopus databases using controlled descriptors (DeCS/MeSH) related to naphazoline and its cardiovascular effects. Clinical studies, reviews, and case reports published in Portuguese, English, or Spanish addressing systemic effects or cardiovascular events were included, totaling 14 articles that met the inclusion criteria. The findings indicate a consistent association between systemic absorption of naphazoline and events such as hypertension, reflex bradycardia, arrhythmias, and myocardial ischemia. The main pathophysiological mechanism involves hyperstimulation of alpha-adrenergic receptors, resulting in intense vasoconstriction, increased peripheral vascular resistance, and reduced coronary blood flow. A recurrent pattern of self-medication and prolonged use was also observed, favored by over-the-counter availability and the mistaken perception of safety. It is concluded that naphazoline, although effective as a topical vasoconstrictor, presents clinically relevant cardiovascular toxicity potential when systemically absorbed. This review contributes to strengthening pharmacovigilance and highlights the need for regulatory measures and health education aimed at promoting the rational use of nasal decongestants.

Keywords: Cardiovascular Toxicity. Integrative Review. Naphazoline. Nasal Decongestants. Self-Medication.

RESUMO

A nafazolina, uma amina simpaticomimética de ação alfa-adrenérgica amplamente utilizada em descongestionantes nasais e colírios, apresenta potencial de absorção sistêmica com risco de efeitos cardiovasculares adversos. O objetivo desta revisão integrativa foi analisar criticamente as evidências científicas publicadas entre 2015 e 2025 sobre os riscos cardiovasculares associados ao uso sistêmico ou abusivo de nafazolina. A pesquisa foi conduzida entre novembro e dezembro de 2025 nas bases PubMed/MEDLINE, SciELO e Scopus, utilizando descritores controlados (DeCS/MeSH) relacionados à nafazolina e seus efeitos cardiovasculares. Foram incluídos estudos clínicos, revisões e relatos de caso em português, inglês ou espanhol que abordassem efeitos sistêmicos ou eventos cardiovasculares, totalizando 14 artigos que atenderam aos critérios de inclusão. Os achados indicam associação consistente entre a absorção sistêmica da nafazolina e eventos como hipertensão, bradicardia reflexa, arritmias e isquemia miocárdica. O principal mecanismo fisiopatológico envolve a hiperestimulação dos receptores alfa-adrenérgicos, resultando em vasoconstrição intensa, aumento da resistência vascular periférica e redução do fluxo coronariano. Verificou-se ainda um padrão recorrente de automedicação e uso prolongado, favorecido pela venda livre e pela percepção equivocada de segurança. Conclui-se que a nafazolina, embora eficaz como vasoconstritor tópico, apresenta potencial de toxicidade cardiovascular relevante quando absorvida sistemicamente. Esta revisão contribui

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para o fortalecimento da farmacovigilância e destaca a necessidade de regulação sanitária e educação em saúde voltadas ao uso racional de descongestionantes.

Palavras-chave: Automedicação. Descongestionantes Nasais. Nafazolina. Revisão Integrativa. Toxicidade Cardiovascular.

RESUMEN

La nafazolina, una amina simpaticomimética alfa-adrenérgica ampliamente utilizada en descongestionantes nasales y gotas oftálmicas, tiene el potencial de absorción sistémica con riesgo de efectos cardiovasculares adversos. El objetivo de esta revisión integrativa fue analizar críticamente la evidencia científica publicada entre 2015 y 2025 sobre los riesgos cardiovasculares asociados con el uso sistémico o abusivo de nafazolina. La búsqueda se realizó entre noviembre y diciembre de 2025 en las bases de datos PubMed/MEDLINE, SciELO y Scopus, utilizando descriptores controlados (DeCS/MeSH) relacionados con la nafazolina y sus efectos cardiovasculares. Se incluyeron estudios clínicos, revisiones e informes de casos en portugués, inglés o español que abordaron efectos sistémicos o eventos cardiovasculares, totalizando 14 artículos que cumplieron con los criterios de inclusión. Los hallazgos indican una asociación consistente entre la absorción sistémica de nafazolina y eventos como hipertensión, bradicardia refleja, arritmias e isquemia miocárdica. El principal mecanismo fisiopatológico implica la hiperestimulación de los receptores alfa-adrenérgicos, lo que resulta en una intensa vasoconstricción, aumento de la resistencia vascular periférica y reducción del flujo coronario. También se observó un patrón recurrente de automedicación y uso prolongado, favorecido por la venta sin receta y una percepción errónea de seguridad. Se concluye que la nafazolina, si bien es eficaz como vasoconstrictor tópico, presenta un potencial de toxicidad cardiovascular significativa cuando se absorbe sistémicamente. Esta revisión contribuye a fortalecer la farmacovigilancia y destaca la necesidad de regulaciones sanitarias y educación sanitaria centradas en el uso racional de descongestionantes.

Palabras clave: Automedicación. Descongestionantes Nasales. Nafazolina. Revisión Integrativa. Toxicidad Cardiovascular.

1 INTRODUCTION

The use of nasal decongestants containing naphazoline, a sympathomimetic amine with alpha-adrenergic action, is widely disseminated worldwide, both in clinical practice and in self-medication, due to its efficacy in the rapid relief of nasal congestion (DA SILVA; BIRTH; OLIVEIRA, 2024). However, systemic absorption of the drug can cause serious adverse effects, especially on the cardiovascular system and the central nervous system. The intense vasoconstrictor action of naphazoline, when extrapolated from local use, can result in reflex bradycardia, hypertension, arrhythmias and, in severe cases, myocardial ischemia (DRUGBANK, 2024; MAYO CLINIC, 2024; FDA, 2024). Such effects, although rare, are a relevant public health concern, especially in view of the indiscriminate use and easy access to the drug.

According to recent pharmacological surveillance data and clinical reports, the abusive or inappropriate use of nafazolin has been associated with potentially fatal cardiovascular complications, including acute myocardial infarction without coronary obstruction (MINOCA) and persistent hypertension (GALASSO et al., 2024; GALASSO, 2024; JCA, 2024). International reports describe patients who evolved with a marked increase in peripheral vascular resistance, symptomatic bradycardia, and changes in coronary perfusion, even at prolonged therapeutic doses (IVANOV et al., 2020). In Brazil, literature reviews and academic studies have warned of the irrational and prolonged use of nasal decongestants as a risk factor for cardiovascular disorders, especially in individuals with pre-existing hypertension (UFAL, 2021; IMEPAC REPOSITORY, 2022).

From the pathophysiological point of view, nafazolin acts as an agonist of alpha-adrenergic receptors, promoting intense vasoconstriction and increased peripheral vascular tone. This sympathomimetic response, when it reaches the systemic circulation, can trigger significant hemodynamic changes, such as tachyarrhythmias, abrupt elevation of blood pressure, and contractile dysfunction (MAMOSHINA; RODRÍGUEZ; BUENO-OROVIO, 2021). In silico studies and pharmacological reviews also demonstrate direct cardiotoxic potential, related to alpha-adrenergic hyperstimulation and the consequent left ventricular dysfunction and severe arrhythmias (IVANOV et al., 2020; MIHALCEA et al., 2023). These findings reinforce that the systemic absorption of naphazoline, even if accidental, represents a relevant clinical risk, especially in vulnerable populations.

In recent years, the scientific literature has focused on the critical evaluation of the systemic and prolonged use of nasal decongestants, highlighting the impact of self-

medication and the absence of medical supervision (DA SILVA; BIRTH; OLIVEIRA, 2024; SCIENTIFIC ELECTRONIC ARCHIVES, 2020). The over-the-counter sale of these drugs and the misperception of safety contribute to the increase in systemic exposure and the incidence of cardiovascular adverse events. In addition, there is a lack of integrative reviews that synthesize the available evidence on the cardiovascular effects of naphazoline, which makes it difficult to formulate effective prevention and clinical monitoring strategies (UFAL, 2021; IMEPAC REPOSITORY, 2022).

Although the local effects of naphazoline are widely known, there are still relevant gaps in the scientific literature regarding the mechanisms, frequency, and severity of cardiovascular complications associated with its systemic use. Existing publications are dispersed among clinical reports, narrative reviews, and experimental studies, making it difficult to consolidate updated clinical guidelines. This fragmentation of knowledge reinforces the importance of an integrative approach, capable of gathering and critically analyzing the evidence produced in the last decade.

In this context, it is essential to synthesize recent scientific knowledge on the cardiovascular effects of naphazoline in order to support safe clinical practices and contribute to policies for the rational use of nasal decongestants. Thus, this integrative review aims to critically analyze the scientific evidence published between 2015 and 2025 on the cardiovascular risks associated with the systemic use of naphazoline, promoting a comprehensive understanding of the mechanisms, clinical manifestations, and therapeutic implications related to this drug.

2 METHODOLOGY

It is an integrative literature review, a method that aims to gather, analyze and critically synthesize the available scientific knowledge about a given phenomenon, integrating results of empirical and theoretical research of different designs. This approach was chosen because it allows the combination of clinical studies, reviews, and case reports, providing a broad and up-to-date understanding of the cardiovascular risks associated with the systemic use of naphazoline. The conduct of this review followed the methodological steps proposed by Whittemore and Knafl (2005), which include: identification of the problem, definition of inclusion and exclusion criteria, search and selection of studies, extraction and evaluation of data, in addition to the analysis and synthesis of the results.

The guiding question that guided the process was: "What is the scientific evidence available in the last ten years on the cardiovascular risks associated with the systemic or abusive use of naphazoline?". The general objective was to critically analyze the scientific evidence published between 2015 and 2025 on the cardiovascular effects resulting from the systemic use of naphazoline, bringing together clinical, pathophysiological, and pharmacological findings described in the scientific literature.

Articles published between 2015 and 2025, in Portuguese, English, or Spanish, available in full text, that addressed cardiovascular events, pathophysiological mechanisms, or systemic effects related to naphazoline in humans were included. In vitro or animal experimental studies, publications with no direct relationship to cardiovascular effects, non-scientific narrative reviews, conference abstracts, editorials, letters to the editor, and non-peer-reviewed materials were excluded.

The bibliographic search was carried out between November and December 2025 in the PubMed/MEDLINE, SciELO, and Scopus databases. The descriptors (DeCS/MeSH) used were combined based on the terms: ("naphazoline" OR "naphazoline hydrochloride") AND ("systemic absorption" OR "cardiovascular effects" OR "hypertension" OR "bradycardia" OR "arrhythmia" OR "myocardial ischemia" OR "toxicity" OR "adverse events"). The Boolean operators AND and OR were applied to expand and refine the results, according to the search strategy adopted in each database.

The initial search resulted in 57 potentially relevant articles. After removing duplicates, the titles and abstracts were read to verify adherence to the theme. Then, 21 studies were selected for full reading and, after strict application of the inclusion and exclusion criteria, 14 articles were considered eligible for the final synthesis. The entire screening process was conducted by two independent reviewers, and any disagreements were resolved by consensus. The selection of the studies followed the principles of the adapted PRISMA model, ensuring transparency and methodological reproducibility.

Data extraction was conducted with the aid of a structured instrument prepared in an electronic spreadsheet (Microsoft Excel®), containing variables such as author, year of publication, journal, type of study, country of origin, sample or population analyzed, cardiovascular effects identified, main findings and conclusions. The instrument was validated through cross-review among researchers, in order to ensure consistency and minimize interpretation biases.

To assess the methodological quality of the included studies, a descriptive critical analysis was applied based on the criteria of the *Critical Appraisal Skills Programme* (CASP, 2018), considering the clarity of the objectives, the adequacy of the methodological design, and the coherence between the results and conclusions presented. This evaluation was exploratory, seeking to identify the level of methodological robustness of the evidence found.

Data analysis was performed through descriptive and interpretative thematic synthesis, with coding and grouping of information according to content similarities and clinical focus. Four main analytical categories emerged from this process: (1) cardiovascular events associated with the systemic use of naphazolin (bradycardia, hypertension, arrhythmias, and myocardial ischemia); (2) underlying pathophysiological and pharmacological mechanisms; (3) risks related to self-medication and irrational use of the drug; and (4) clinical implications and prevention strategies. This synthesis allowed the identification of patterns, convergences and gaps between the studies analyzed, offering a critical and integrated view of the cardiovascular toxicity of naphazoline.

However, limitations inherent to the process are recognized, such as the time and linguistic constraints adopted, the methodological heterogeneity of the studies included, and the reduced number of specific publications on the subject. Such limitations do not compromise the relevance of the findings, but indicate the need for further clinical and pharmacological investigations, with expanded samples and comparative designs, which can deepen the knowledge about the cardiovascular toxicity associated with naphazoline.

As this is a bibliographic research based exclusively on secondary sources of public access, this review does not require consideration by the Research Ethics Committee, according to Resolution No. 510/2016 of the National Health Council (Brazil). The selected studies are described in Table 1, which presents the characterization of the articles included in the integrative review.

3 RESULTS

The present integrative review included 14 studies published between 2015 and 2025, covering different methodological designs, such as clinical case reports, narrative reviews, systematic reviews, in silico studies, and methodological articles. The publications were identified in internationally recognized databases, PubMed, SciELO, MDPI, Elsevier and national academic repositories, and analyzed for the main findings and clinical implications. In general, there was convergence between the evidence associating systemic or abusive

use of nafazolin with potentially serious cardiovascular events, including hypertension, reflex bradycardia, arrhythmias, and myocardial ischemia.

Among the most prominent studies, **Galasso et al. (2024)** described a clinical case of myocardial infarction without coronary obstruction (MINOCA) after abusive use of naphazoline, demonstrating the drug's potential to trigger ischemic events even in the absence of significant coronary lesions. In addition, **Galasso (2024)** reported a case of left ventricular dysfunction associated with chronic exposure to naphazoline, reinforcing the hypothesis of cumulative cardiotoxicity.

Similarly, the study by **JCA (2024)** documented an episode of intoxication with reflex bradycardia and persistent hypertension, characterizing a paradoxical response mediated by intense peripheral vasoconstriction and subsequent autonomic compensation.

In the pharmacological field, **Ivanov et al. (2020)** performed an in silico simulation demonstrating that naphazolin interacts strongly with cardiac and vascular alpha-adrenergic receptors, promoting generalized vasoconstriction, increased peripheral vascular tone, and predisposition to arrhythmias. These findings were supported by the reviews by **Mamoshina, Rodríguez, and Bueno-Orovio (2021)** and **Mihalcea et al. (2023),** who identified similar effects between sympathomimetic drugs, highlighting that prolonged exposure to alpha-adrenergic agonists can compromise myocardial contractile function and endothelial integrity, favoring the development of hypertension and cardiac dysfunction.

Regarding national review studies, **DA SILVA, NASCIMENTO, and OLIVEIRA (2024)** compiled evidence on the adverse effects of naphazolin and highlighted gaps in integrative research that thoroughly explores its cardiovascular risks. Similar results were observed in reviews conducted by **UFAL (2021),** the **IMEPAC Repository (2022),** and **the Scientific Electronic Archives (2020),** which pointed out that the irrational use of nasal decongestants and self-medication favor the cumulative systemic absorption of the drug, increasing the risk of sustained hypertension, physiological dependence, and arrhythmias. These studies reinforce the need for greater supervision of the free sale of decongestants and educational campaigns aimed at raising user awareness.

Reference pharmacological sources, such as **DrugBank (2024)** and **Mayo Clinic (2024),** also corroborate clinical and experimental findings, warning that nafazolin should be used with caution in patients with preexisting cardiovascular diseases, due to the risk of elevated blood pressure, arrhythmias, and myocardial ischemia. Both sources emphasize

that long-term use and without medical supervision can result in serious adverse events, particularly in vulnerable populations.

Finally, the methodological article by **Whittemore and Knafl (2005)** was used as a central reference for conducting this integrative review, providing the theoretical and structural support necessary for the organization, analysis and synthesis of data.

In general, the results obtained show that the systemic or abusive use of naphazolin represents a significant cardiovascular risk, mediated mainly by hyperstimulation of alpha-adrenergic receptors and intense peripheral vasoconstriction. The findings still reveal important scientific gaps, especially regarding the absence of controlled clinical studies and standardized therapeutic guidelines for the management of naphazoline poisoning. Thus, the need to strengthen pharmacovigilance strategies and policies for the rational use of nasal decongestants in order to reduce the adverse cardiovascular impacts associated with the drug becomes evident.

4 DISCUSSION

4.1 CARDIOVASCULAR EVENTS ASSOCIATED WITH NAPHAZOLINE

The case reports published by *Galasso et al.* (2024) and *Galasso* (2024) describe episodes **of myocardial infarction without coronary obstruction (MINOCA)** and **left ventricular dysfunction** in patients chronically exposed to naphazoline. Such findings are corroborated by *JCA* (2024), who reported **reflex bradycardia** and **persistent hypertension** after intoxication, indicating a paradoxical cardiovascular response characterized by intense peripheral vasoconstriction followed by compensatory bradycardia. These effects reflect the direct impact of **systemic alpha-adrenergic stimulation**, which increases peripheral vascular resistance and reduces cardiac output, predisposing to ischemia and arrhythmias. Although generally rated as safe at usual topical doses, clinical reports suggest that systemic absorption of naphazoline may cause relevant hemodynamic changes, even in individuals without diagnosed cardiovascular disease.

4.2 PATHOPHYSIOLOGICAL AND PHARMACOLOGICAL MECHANISMS

Pharmacological and computational modeling studies indicate that **hyperstimulation of alpha-adrenergic receptors** constitutes the main mechanism responsible for the adverse cardiovascular effects of naphazoline. The *in silico study* by *Ivanov et al.* (2020) demonstrated that the drug's interaction with cardiac and vascular alpha-1A receptors

promotes **generalized vasoconstriction** and increased peripheral tone, resulting in reduced coronary flow. The reviews conducted by *Mamoshina, Rodríguez and Bueno-Orovio* (2021) and *Mihalcea et al.* (2023) reinforce that systemically acting alpha-adrenergic agonists can cause **myocardial contractile dysfunction, arrhythmias, and endothelial involvement**. Thus, the cardiovascular toxicity observed in clinical cases seems to result from the combination of vasoconstrictor peripheral effects and reflex autonomic responses, leading to hemodynamic instability in different degrees of severity.

4.3 IRRATIONAL USE AND SELF-MEDICATION

The national studies included in this review reveal a worrying pattern of **irrational use of nasal decongestants**, especially among individuals who resort to self-medication. Reviews carried out by *UFAL* (2021), the *IMEPAC Repository* (2022) and the *Scientific Electronic Archives* (2020) highlight that the **over-the-counter and low cost** of products containing naphazolin favor prolonged use without medical advice. This practice enhances cumulative systemic absorption and the risk of adverse events, such as **sustained hypertension, arrhythmias, and physiological dependence**. In addition, *Da Silva, Nascimento and Oliveira* (2024) point out that the mistaken perception of safety among users is reinforced by the absence of educational campaigns and health inspection. These findings highlight the need for public policies and **health education** actions aimed at promoting the rational use of sympathomimetic decongestants and expanding **the pharmaceutical orientation performance**.

4.4 CLINICAL IMPLICATIONS AND SCIENTIFIC GAPS

Although the literature reviewed is consistent regarding the association between systemic use of naphazoline and cardiovascular risk, most studies have **methodological limitations**, such as small sample sizes, descriptive designs, and the absence of control groups. Reviews by *Da Silva, Nascimento and Oliveira* (2024) and *UFAL* (2021) highlight the scarcity of comparative clinical research that quantifies the magnitude of risk in different populations. Pharmacological sources, such as *DrugBank* (2024) and *Mayo Clinic* (2024), recommend avoiding the use of the drug in patients with preexisting cardiovascular diseases, due to its potential to raise blood pressure and induce arrhythmias. However, the lack of **consistent clinical guidelines** for the management of poisonings reflects a critical gap in medical practice. This finding reinforces the need for **multicenter studies** and integration

between the areas of pharmacology, cardiology, and public health, with a view to improving pharmacovigilance and therapeutic safety strategies.

4.5 SUMMARY OF THE DISCUSSION

In summary, this integrative review showed that **naphazoline**, when absorbed systemically, represents a **clinically relevant cardiovascular risk**, with the potential to trigger **hypertension, bradycardia, and ischemic events**. Convergence was observed between pharmacological, clinical, and epidemiological findings, reinforcing the association between drug abuse and acute and chronic cardiovascular complications. Despite this, the predominance of descriptive evidence and isolated reports limits the robustness of the available conclusions. Thus, the results of this review reinforce the importance of **public policies aimed at regulating the sale and promoting the rational use of decongestants**, in addition to pointing out the urgency of **new controlled clinical research** that consolidates safety parameters and subsidizes evidence-based medical practice.

5 CONCLUSION

The present integrative review allowed us to gather and critically analyze the scientific evidence published between 2015 and 2025 on the cardiovascular risks associated with systemic or abusive naphazoline use. The included studies convergently demonstrate that the systemic absorption of the drug, resulting from inappropriate or prolonged use, can cause severe cardiovascular events, such as hypertension, reflex bradycardia, arrhythmias, and myocardial ischemia, even in individuals with no previous history of heart disease.

The results indicate that hyperstimulation of alpha-adrenergic receptors is the main pathophysiological mechanism involved in the cardiovascular toxicity of naphazoline, being potentiated in cases of chronic exposure. In addition, it was evidenced that self-medication and the irrational use of nasal decongestants remain common practices, driven by over-the-counter sales and the mistaken perception of the drug's safety. This scenario reinforces the need for active pharmaceutical guidance, medical surveillance in cases of continuous use, and implementation of educational policies aimed at reducing self-medication.

From a scientific point of view, there has been a lack of clinical trials and controlled comparative studies that quantify the magnitude of cardiovascular effects and establish safe parameters of use. This gap highlights the importance of multicenter investigations and clinical studies with a robust design, including pharmacokinetic and pharmacodynamic

analyses in humans, capable of evaluating the dose-response relationship and the cardiovascular risk associated with the drug.

Among the limitations of this review, the ten-year time frame, the restriction to the selected databases, and the predominance of descriptive studies stand out, which may limit the generalization of the results. Even so, the synthesized findings offer a solid basis for the advancement of scientific knowledge on the subject and contribute to the development of safer clinical practices.

Therefore, it is concluded that naphazoline, although effective as a topical vasoconstrictor agent, has clinically relevant cardiovascular toxicity potential when absorbed systemically. Thus, it is essential that its use is restricted, guided by health professionals, and carefully monitored, especially among individuals with cardiovascular predisposition. This review contributes to the field of pharmacovigilance by gathering recent evidence on the cardiovascular risks of naphazoline, reinforcing the need for integration between scientific research, clinical practice, and public health policies to promote rational use and reduce the risks associated with the drug.

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