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Effectiveness of Nitrate and Beta-Blocker Drugs in Patients with Angina Pectoris: A Systematic Literature Review

Maya Arfania[1], Adinda Khoirun Nissa[1], Khoirul Haniatin[1], Novita Andriyani[1*]

[1]Pharmacy Study Program, Faculty of Pharmacy, Universitas Buana Perjuangan Karawang, Karawang, Indonesia

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***Corresponding author:**
Novita Andriyani

E-mail address:
novitaandriyani999@gmail.com

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A B S T R A C T

Angina pectoris is the most common clinical manifestation of myocardial ischemia and often occurs when the heart needs more blood. The main goals of treatment in patients with unstable angina are relief of symptoms, slowing disease progression, and reducing future events, especially myocardial infarction, and death. This study aimed to explore the literature regarding the effectiveness of nitrate and beta-blocker drugs in angina pectoris patients. The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding risk factors and clinical overview of acute kidney injury. The search was performed using the terms: (1) "nitric oxide" OR "beta-blockers" OR "morbidity" OR "mortality" AND (2) "angina pectoris". The literature is limited to clinical studies and published in English. Sublingual nitroglycerin has become the mainstay of treatment for angina pectoris. This drug can be used to relieve acute angina or as a prophylaxis, namely before activities that can trigger angina. Beta-blockers are a type of drug that can be used to relieve angina symptoms and prevent ischemic events through the mechanism of reducing myocardial oxygen demand, reducing heart rate, and myocardial contractility. These drugs work by competitively inhibiting the action of circulating catecholamines at cell membrane beta-adrenergic receptors. In conclusion, nitrate and beta-blocker drugs are the main choices in relieving angina pectoris symptoms.

1. Introduction

Angina is a common presenting symptom (usually chest pain) among patients with coronary artery disease. Myocardial ischemia develops when coronary blood flow becomes inadequate to meet myocardial oxygen demands. Angina pectoris is the most common clinical manifestation of myocardial ischemia and often occurs when the heart needs more blood. Angina commonly occurs during exercise, strong emotions, or exposure to extreme temperatures. Some people, such as those with coronary artery spasms, may experience angina at rest. Angina is a sign that a person is at high risk of having a heart attack, cardiac arrest, or sudden cardiac death.[1,2]

In people with unstable angina, unexpected chest pain is the most common symptom. The discomfort may be more severe and prolonged than usual angina, or it may be the first time a person has angina. The most common cause is reduced blood flow to the heart muscle due to the narrowing of the coronary arteries by atherosclerosis. The artery may be abnormally narrowed or partially blocked by a blood clot. Inflammation, infection, and other secondary causes can also cause unstable angina. The main goals of treatment in patients with unstable angina are relief of symptoms, slowing disease progression, and reducing future events, especially myocardial infarction, and death.[3,4] This study aimed to explore the literature

regarding the effectiveness of nitrate and beta-blocker drugs in angina pectoris patients.

2. Methods

The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding risk factors and clinical overview of acute kidney injury. The search was performed using the terms: (1) "nitric oxide" OR "beta-blockers" OR "morbidity" OR "mortality" AND (2) "angina pectoris". The literature is limited to clinical studies and published in English. The literature selection criteria are articles published in the form of original articles, an observational study about the effectiveness of nitrate and beta-blocker drugs in angina pectoris patients, studies were conducted in a timeframe from 2000-2023, and the main outcome was morbidity and mortality of angina pectoris. Meanwhile, the exclusion criteria were studies that were not related to angina pectoris, the absence of a control group, and duplication of publications. This study follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA) recommendations.

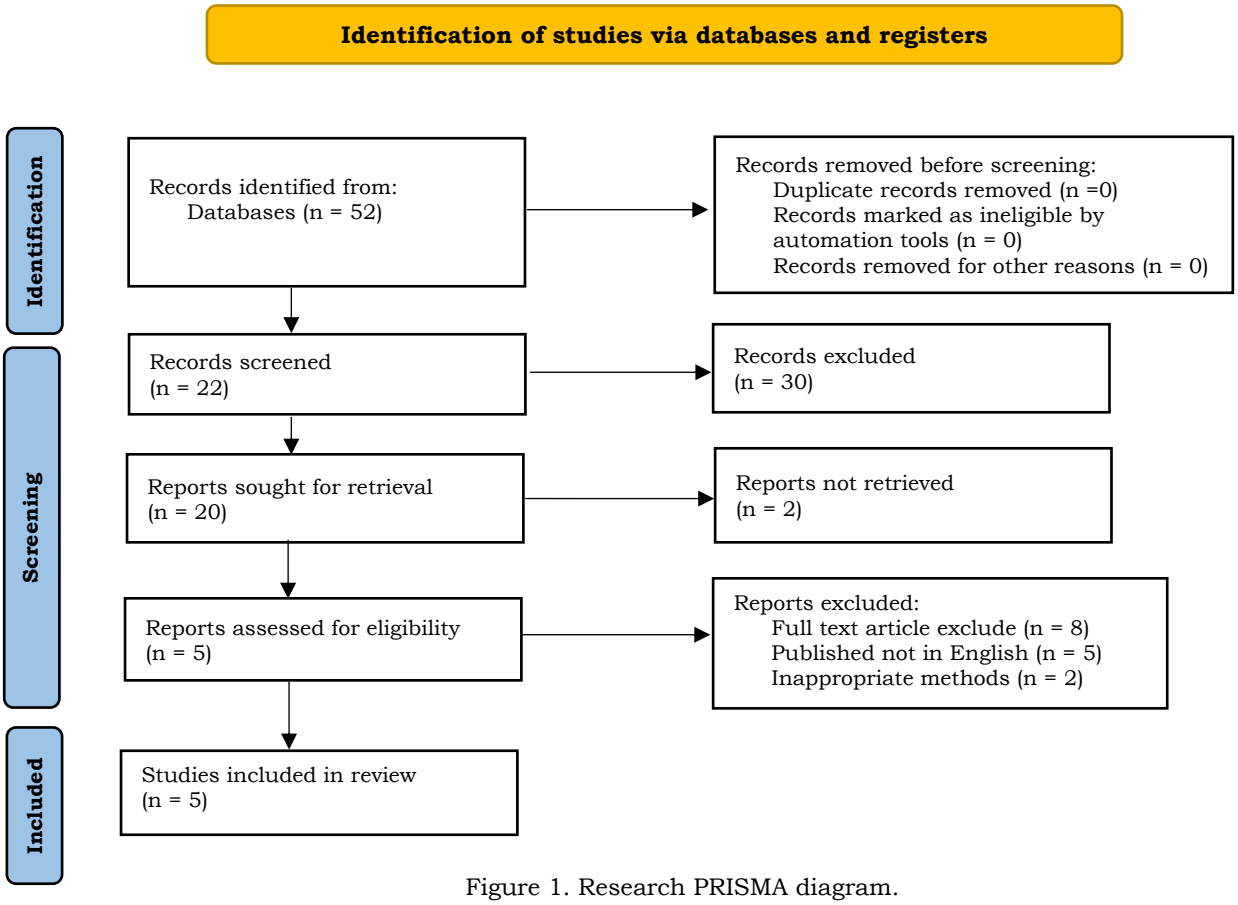

Figure 1. Research PRISMA diagram.

3. Results and Discussion

The role of nitrate drugs in angina pectoris

Nitric oxide is a potent vasodilator that induces the formation of cyclic guanosine monophosphate (cGMP) by activating soluble guanylyl cyclase (sGC) in vascular smooth muscle cells.[4] cGMP can bind and enhance the activity of protein kinase G, cGMP-gated ion channels, and cGMP-sensitive phosphodiesterase. G protein kinase promotes cytosolic calcium reuptake into the sarcoplasmic reticulum, movement of calcium from the intracellular to extracellular environment, and opening of calcium-activated potassium channels.

These changes result in the relaxation of vascular tone because decreased intracellular calcium impairs the ability of myosin light chain kinase to phosphorylate myosin, resulting in the relaxation of smooth muscle cells.[5,6]

Organic nitrates, such as nitroglycerin, isosorbide dinitrate, and isosorbide mononitrate, are absorbed rapidly from several sites, such as the gastrointestinal tract, mucous membranes, and skin, depending on the preparation. This compound is a prodrug with a nitrooxy group (-O-NO_2) and is metabolized to produce bioactive metabolites. Bioactivation of organic nitrates leads to the release of NO, which allows them to function as NO donors. Nitric oxide then causes vasodilation through its effect on vascular smooth muscle cells and impairs platelet activation. Nitrates also cause vasodilation through other indirect mechanisms. Nitroglycerin has been shown to increase the activity of histone acetylases with a nitroglycerin-dependent vascular response influenced by Nε-lysine acetylation of contractile proteins.[7,8]

Sublingual nitroglycerin has become the mainstay of treatment for angina pectoris. This drug can be used to relieve acute angina or as a prophylaxis, namely before activities that can trigger angina. There is no evidence that long-acting nitrates improve survival in patients with coronary artery disease. Treatment with nitrates causes capacitance venous vasodilation and results in a decrease in ventricular filling pressure, wall tension, and myocardial oxygen demand. Nitroglycerin is the drug most often used to treat acute episodes of angina. It is usually given as a sublingual tablet but is also available as a sublingual spray. Nitroglycerin oral spray or sublingual nitroglycerin can also be used before angina-inducing activities to prevent acute angina from occurring.[9]

One major problem with the use of nitrates is the development of drug tolerance, resulting in the loss of hemodynamic and antianginal effects during continued therapy. Tolerance occurs after chronic exposure to all classes of nitrates and results in a complete or marked reduction of antianginal and anti-ischemic effects over a 24-hour period of long-term therapy. Pseudotolerance is also an issue that complicates chronic treatment with organic nitrates. This adaptive phenomenon is not considered true vascular tolerance because it occurs in response to any form of vasodilator therapy. Pseudotolerance is characterized by neurohormonal activation, increased rate of catecholamine release and circulating catecholamine levels, sodium retention, and intravascular volume expansion.[8,9]

The role of beta blocker drugs in angina pectoris

Beta-blockers are a type of drug that can be used to relieve angina symptoms and prevent ischemic events through the mechanism of reducing myocardial oxygen demand, reducing heart rate, and myocardial contractility. These drugs work by competitively inhibiting the action of circulating catecholamines at cell membrane beta-adrenergic receptors. Beta-blockers are recommended by the European Society of Cardiology as first-line antianginal therapy to reduce heart rate (HR) and symptoms in patients with chronic coronary syndromes. Previous studies have shown beta-blockers reduce mortality and morbidity after acute myocardial infarction.[10,11]

By inhibiting beta-receptor activation leading to decreased inotropy and sinus velocity and slowing atrioventricular (AV) conduction, beta-blockers are effective for relieving angina symptoms and preventing ischemic events.[12-15] Reduction in resting and exercise heart rate, contractility, and arterial pressure with beta-blockers can lead to decreased myocardial oxygen demand.[13] Decreasing heart rate increases diastolic perfusion time, which can increase left ventricular (LV) perfusion.[14-17] However, there are also some side effects of beta-blockers, such as physical and mental fatigue, nightmares, nausea, impotence, cold extremities, and decreased patient adherence to taking medication. The most serious side effects are heart failure, heart block, and bronchospasm. Other milder side effects include tiredness and cold extremities.[18-20]

4. Conclusion

Nitrate and beta-blocker drugs are the main choices that are effective in relieving angina pectoris symptoms.

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