ANGINA PECTORIS: A REVIEW ON CURRENT AND FUTURE TREATMENT STRATEGIES

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Abstract

Angina pectoris affects about 9 million people in the U.S. with the most frequent symptom. Developing techniques to improve the management of chronic stable angina remains a priority. Obesity, diabetes, hypertension, high cholesterol, a smoking history, and a family history of chronic renal disease are all potential causesThe majority of persons with angina have one or more substantially constricted epicardial coronary arteries. A less common cause is coronary artery vasospasm .Cold weather, activity, or medications that induce vasoconstriction, such as alpha-agonists, can produce spasms. Myocardial ischaemia may continue or return in a small percentage of people after successful coronary revascularization. Maintaining or achieving a healthy weight is crucial. In high-risk individuals, a 'Mediterranean diet' supplemented with extra-virgin olive oil or almonds decreases MACE. Exercise can help alleviate discomfort and improve the prognosis. Managing or lowering heart rate spikes is critical in the treatment of angina pectoris. For AP patients, SIHD treatment guidelines propose beta-blockers (BBs) as first-line medication. For AP patients, SIHD treatment guidelines propose beta-blockers (BBs) as first-line medication.

Keywords: Coronary arteries, Angina pectoris, Heart Rate, Ivabradine

Introduction

Ischaemic heart disease and angina pectoris continues to be the major cause of death and disability in Western countries. Angina pectoris, which affects about 9 million people in the U.S., is the most frequent symptom. Developing techniques to improve the management of chronic stable angina remains a priority.[1] Lifestyle adjustments are being employed to prevent or reduce the progression of atherosclerosis. When compared to placebo, antianginal medicines are licensed for clinical use if they improve walking effort time to angina. Although highly recommended, cardiovascular outcomes are not required for regulatory approval and antianginal medicines, on the other hand, have yet to be proven to lower cardiovascular mortality, heart attack or stroke risk.[2]

Epidemiological Studies

More than 40% of people with suggestive symptoms of obstructive coronary artery disease have normal coronary arteries. Many studies have shown that microvascular angina (MVA) is caused by microcirculatory dysfunction.

MVA does not always present with a stable angina pattern that is effort-related.[2] Chronic stable angina affects around 30000 to 40000 people per million in Western countries. The incidence of both males and females increases with age. Risk factors include obesity, diabetes, hypertension, high cholesterol, a history of smoking, cocaine or amphetamine addiction, and a family history of chronic renal illness[3].

Types of Angina Pectoris:-

Table 1: Etiology and Symptoms of Different Types of Angina Pectoris

S. No	Types of Angina Pectoris	Etiology of Angina Pectoris	Symptoms of angina pectoris
1	STABLE ANGINA	➢ Although the exact origin of stable angina is uncertain, it is thought to be caused by an imbalance in myocardial supply and demand. ➢ The majority of persons with angina have one or more substantially constricted epicardial coronary arteries. According to study, many persons with stable angina have non-obstructive or even normal coronary arteries.[4]	➢ Fatigue. ➢ Dizziness. ➢ Rapid Breathing. ➢ Nausea. ➢ Heart palpitations. ➢ Sweating. ➢ Anxiety ➢ Exercise/physical activities, such as climbing flights of stairs.
2	UNSTABLE ANGINA	➢ Coronary atherosclerosis is the underlying cause of unstable angina in nearly all patients with acute myocardial ischemia. ➢ Coronary artery constriction produced by a nonocclusive thrombus that originates on a disturbed atherosclerotic plaque is the most common cause of unstable angina. ➢ A less common cause is coronary artery vasospasm (variant	➢ Nausea ➢ Vomiting ➢ Diaphoresis ➢ Dizziness ➢ Palpitations ➢ Tightness ➢ Burning ➢ Sharp type of pain

		Prinzmetal angina). Endothelial or vascular smooth muscle dysfunction causes this vasospasm.[5]	
3	VARIANT ANGINA	➢ A widespread or segmental spasm in the coronary arteries causes Printzmetal angina. ➢ A decrease in blood supply to the myocardium generate symptoms such as chest pain. Cold weather, activity, or medications that induce vaso-constriction, such as alpha-agonists, can produce spasms in the coronary arteries	➢ Usually occurs while resting and during the night or early morning hours ➢ Are usually severe ➢ Can be relieved by taking medication
4	MICROVASCULAR ANGINA	➢ In coronary small vessel disease, the smallest arteries do not relax (dilate) as they should. As a result, the heart does not receive enough oxygen-rich blood. According to clinicans, small vessel ailment is caused by the same factors as problems affecting the larger arteries of the heart, such as high blood pressure, high cholesterol, obesity, and diabetes.	➢ Chest discomfort ➢ Dyspnea ➢ Tirdeness and lack of energy

Pathophysiology of Angina Pectoris

a) Causes of Chest Pain:-Non-cardiac chest pain can be caused by gastroesophageal reflux disease, musculoskeletal alterations, pulmonary and aortic abnormalities, and mental health issues. Many people have coronary angiography as a result of chest pain syndromes.[6]

b) Angina with Epicardial Coronary Disease:-Angina is a heart disorder caused by a mismatch in the supply of oxygen to myocytes and the demand for oxygen in

myocardium. Exercise or mental stress-induced ischaemia can cause angina symptoms in those with atherosclerotic CAD in the main coronary arteries. Because angina pain is complex and has a convoluted link with ischaemia, the ultimate source of pain is controversial. Several ganglia are located in the heart, predominantly in the epicardial fat, and are supplied by the proximal coronary arteries.

c) Angina without Epicardial Coronary Artery Obstruction:-Angina has been refuted because epicardial stenosis reduces coronary flow reserve. Myocardial ischaemia may continue or return in a small percentage of people after successful coronary revascularization.

d) Pathogenesis of Coronary Microvascular Dysfunction:-Endothelial dysfunction is a malfunction of the endothelial cells in the microvascular network. Increased oxidative stress results in the formation of thromboxane A2, prostaglandin H2, and superoxide, which constricts the dilator response to different stimuli.

Prevention of Angina Pectoris

1. Lifestyle modification:

- Tobacco smoking, including environmental exposure, must be avoided, as the benefits of quitting smoking have been well established. Maintaining or achieving a healthy weight is crucial.
- A 'Mediterranean diet' supplemented with extra-virgin olive oil or almonds reduces MACE in high-risk patients. Blood pressure (BP) control is crucial in both risk management and angina treatment. Exercise training can help relieve symptoms and improve the prognosis.
- Treatment of hypercholesterolemia, particularly reducing LDL-cholesterol levels with a statin, reduces the chance of adverse effects.[7]

2. Pharmaceutical agents:

- Angina is a symptomatic manifestation of complex physiological processes and can be manipulated pharmacologically through multiple pathways. Some agents have been available for decades, while recent advancements have brought newer, better tolerated, or even more effective alternatives to the patient's standard of care.
- By employing indirect strategies such as blood pressure reduction.
- It has an anti-arrhythmic nature.
- The findings suggest that those with left ventricular dysfunction and a hazard ratio of fewer than 70 beats per minute, with or without angina, may benefit from the treatment.[8]
- MACE is reduced in specific patient groups, but not in the vast majority of chronic stable angina patients.[9]

3. lowered heart rate :-

- Lowering or managing heart rate spikes is crucial in the therapy of AP.
- A faster heart rate suggests a greater risk of cardiovascular illness. To reduce heart rate, drugs that directly block the sinus node channel without changing blood pressure or contractility are utilised.

Diagnosis of Angina Pectoris

A. ECG (electrocardiogram) test:- This test analyses your heart's electrical activity and rhythm.
B. Stress test:-A stress test is an exercise that puts you under a huge strain, this checks the activity of your heart during exercise
C. Blood test:-Blood tests are a sort of test that is performed to assess a person's health A significant number of them are released when your heart muscle is harmed, such as during a heart attack. Your doctor may request more comprehensive testing, such as a metabolic panel or a full blood count (CBC).[10]
D. Imaging tests:-These are a subcategory of imaging testing.Chest X-rays help rule out other issues that might be causing your chest pain, such as lung illnesses. Echocardiograms, CT scans, and MRI scans can all offer images of your heart that can help your doctor diagnose the problem.The heart is catheterized, in this the clinicans will put a long, thin tube into an artery in your leg and thread it up to your heart to measure your blood flow and pressure.
E. Coronary angiography:- it is the examination of the coronary arteries in this the clinicans will inject a dye into the blood vessels of heart
F. Physical examination

Treatment of Angina Pectoris

1. MEDICATION:-

A. Beta - Blocker (BBs): Adrenergic blocking agents i.e, beta -blocker(BBs) diminish the increase in heart rate caused by physical and emotional stress. They enhance ischemic area perfusion by shifting microvascular flow. SIHD management guidelines recommend BBs as first-line therapy for AP patients.[11]

B. Sinus node inhibitors: These are the substances that inhibit the sinus node and Ivabradine works as a sinus node inhibitor. It reduces the heart rate by blocking the pacemaking current of the sinus nodes. The guidelines have not been altered since they were approved by the FDA.

C. Amiodarone and dronedarone: Amiodarone and its derivative dronedarone are complex compounds that have a number of cardiovascular effects, including a reduction in heart rate owing to multi-channel blockage. A randomised, double-blind, placebo-controlled trial demonstrated extraordinary improvement in patients with New York Class Association Class 3 stable AP and abnormal exercise treadmill tests [12]. Dronedarone, an iodine-free methane-sulfonyl group derivative with a lower side effect profile, has not been extensively studied as an anti-anginal medication. It significantly decreased acute coronary syndromes and hospitalisation costs in elderly people with atrial fibrillation.[13]

D. Smooth muscle Relaxant: The relaxation of vascular smooth muscle is controlled by a signalling cascade that includes nitric oxide (NO), S-nitrosothiol, and cyclic guanylate cyclase. Various chemicals regulate this pathway by blocking or boosting different stages of the cascade.

E. Nitrate preparations:-These are useful both alone and in combination with CAs for the relief/prevention of angina induced by coronary spasm. The most common side effect is headache, which affects up to 50% of all patients. Patients using phosphodiesterase inhibitors (PDEi) and those suffering from hypotension should take caution.[14]

F. Phosphodiesterase inhibitors:-The motivation for the creation of phosphodiesterase inhibitors came from anti-anginal medications (PDEi). The mechanism of action is a reduction in cyclic guanyl monophosphate (cGMP) metabolism, which amplifies the effects of endogenous NO. Later studies confirmed a beneficial impact on the pulmonary vascular system, adding to the list of pulmonary hypertension therapies.[15]

2. Revascularization procedures:-

a. Enhanced external counterpulsation
b. Transmyocardial revascularization
c. Stem cell therapy[16]

i. **Enhanced external counter pulsation:** Enhanced external counter pulsation (EECP) is the only truly noninvasive and safe intervention for which a reduction of angina symptoms and nitrate use, increased exercise tolerance, and improvement in myocardial ischaemia [17]
ii. **Trans-myocardial laser revascularization:** TMR emerged as treatment modality for patients with diffuse coronary artery disease not amendable to percutaneous or surgical revascularization. The procedure entails the creation of laser channels within ischemic myocardium in an effort to better perfuse these areas.[18]
iii. **Stem cell therapy:** This therapy is emerged as a potential therapeutic option for these patients. It is an experimental therapy involving stem cell injections from the patient's own blood is showing promise in the treatment of people with chest pain that is not responsive to drugs, angioplasty, or surgery[19]

Future Aspects:- Despite its broad list of adverse effects, ranolazine is currently being used as a novel therapeutic option for angina that has proven resistant to traditional therapies.[20] Invasive treatments such as spinal cord stimulation and laser revascularization may give additional benefits as secondary therapeutic options.[21]

Conclusion

Chronic stable angina pectoris affects around 30000 to 40000 people per million in Western countries. Risk factors include obesity, diabetes, hypertension, high cholesterol, a smoking history and a family history of chronic renal disease. Patients with stable angina pectoris are frequently advised for cardiac catheterization without making a genuine effort to address their symptoms with conventional treatment and with proper treatment, many patients may have gone asymptomatic and avoided catheterizations and subsequent percutaneous operations.

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Conflicts of Interest:

There are no conflicts of interest among the authors

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