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UNSTABLE ANGINA, LITERATURE REVIEW

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SUMMARY

Introduction: *Angina, or chest pain, is the most frequent symptom of ischemic heart disease, one of the primary origins of morbidity and mortality worldwide. Unstable angina falls within a spectrum under the general term acute coronary syndrome, being the leading cause of death worldwide.*
Objective: *to detail current information related to unstable angina, definition, etiology, epidemiology, anamnesis, physical examination, evaluation, treatment and prevention.*
Methodology: *a total of 28 articles were analyzed in this review, including review and original articles, as well as clinical cases, of which 16 bibliographies were used because the other articles were not relevant to this study. The sources of information were PubMed, Google Scholar and Cochrane; the terms used to search for information in Spanish, Portuguese and English were: angina, precordial pain, cardiac management, unstable angina, cardiac emergencies, treatment.*

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Results: *Coronary artery disease is estimated to cause more than one third of deaths in individuals over 35 years of age. It is the leading cause of death in this age group. The incidence is more frequent in men; however, as individuals exceed 75 years of age, the incidence between men and women becomes more balanced. The average age of presentation is 62 years. The basis of treatment focuses on improving coronary artery perfusion.*

Conclusions: *Unstable angina is characterized by an onset during rest, its diagnosis is clinical so it is of vital importance to know its clinical, epidemiological manifestations and its evaluation to reach a correct diagnosis, in order to guarantee a timely and adequate treatment. Since this condition continues to be a public health problem that affects a high percentage of the population on a daily basis, it is important to raise awareness of the problem and to try to prevent it by modifying lifestyle.*

KEY WORDS: *angina, precordial pain, cardiology.*

INTRODUCTION

Angina, or chest pain, is the most frequent symptom of ischemic heart disease, one of the primary sources of morbidity and mortality worldwide. Chest pain can be due to cardiac and non-cardiac pathologies. Adequate anamnesis and physical examination are essential to differentiate between these origins and to identify individuals with acute coronary syndrome. Angina is one of the signs of acute coronary syndrome (ACS) and can be classified into stable and unstable angina. Stable angina is defined as the appearance of symptoms only with exertion, while in the case of unstable angina, symptoms appear at rest and require early assessment and appropriate management(1,2).

Unstable angina falls within a spectrum under the general term acute coronary syndrome. It is a public health problem that disturbs many people in the world on a daily basis and has become the leading cause of death worldwide. It is paramount to distinguish between this and several other sources of chest pain including stable angina. Health care providers should be aware of the signs and symptoms of acute coronary syndrome, because affected individuals rely on them to distinguish it from other sources of precordial pain. Usually affected individuals with symptomatology are directed to the emergency room, however, acute coronary syndrome can also present in the outpatient setting. Over time, a significant amount of research has been conducted to demonstrate the most effective and appropriate treatment modalities and diagnostic materials available to assess unstable angina and other variants of acute coronary syndrome(3-5).

METHODOLOGY

A total of 28 articles were analyzed in this review, including review and original articles, as well as cases and clinical trials, of which 16 bibliographies were used because the information collected was not sufficiently important to be included in this study. The sources of information were Cochrane, PubMed and Google Scholar; the terms used to search for information in Spanish, Portuguese and English were: angina, precordial pain, cardiac management, unstable angina, cardiac emergencies, treatment.

The choice of literature exposes elements related to unstable angina, definition, etiology, epidemiology, anamnesis, physical examination, evaluation, treatment and prevention.

DEVELOPMENT

Definition

Unstable angina is defined as myocardial ischemia at rest or minimal effort, in the absence of cardiomyocyte necrosis, as evidenced by the non release of cardiac biomarkers of myocardial necrosis into the circulation. With clinical diagnosis and is characterized by its onset at rest, with progressive intensity and recent onset(6).

Etiology

Chest pain can be of non-cardiac origin, from nonischemic heart disease, as well as from ischemic heart disease. Non-cardiac causes include gastroesophageal reflux disease, musculoskeletal causes, pulmonary disease and anxiety/panic attacks. Non-ischemic cardiac causes include pericardial disease. It is now widely accepted that the etiology of chest pain caused by cardiac ischemia is due to coronary artery atherosclerosis and coronary vasospasm. This condition leads to a mismatch between myocardial oxygen supply and demand. In stable angina, the increase in demand only occurs with exertion; on the other hand, in unstable angina it also occurs at rest. The increase in myocardial oxygen demand due to exercise is primarily due to increased blood pressure, heart rate and myocardial contractility, as well as other factors. In normal cardiac physiological conditions, the increase in oxygen demand generated by exertion and consequent coronary vasodilatation, however in cases of coronary artery atherosclerosis, this function is interrupted, leading to ischemia and chest pain(1,2,7,8).

Coronary atherosclerotic disease is the underlying reason for unstable angina in most individuals with acute myocardial ischemia. The most common origin of unstable angina is due to coronary artery narrowing caused by a thrombus that develops over a ruptured atherosclerotic plaque and is not occlusive.

A less common origin is vasospasm of a coronary artery (Prinzmetal's angina variant), due to endothelial or vascular smooth dysfunction(3,9).

Epidemiology

Coronary artery disease is present in a large part of the population. It is estimated that coronary artery disease causes more than one third of deaths in individuals over 35 years of age. It is the leading cause of death in this age group. It is estimated that around 18

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million people in the USA alone are affected by this disease. The incidence is more frequent in men, however, as individuals exceed 75 years of age, the incidence between men and women becomes more balanced. Other risk factors are family history, obesity, high cholesterol, smoking, diabetes, hypertension, cocaine or amphetamine abuse, HIV, autoimmune disorders, anemia and chronic kidney disease. The mean age of presentation is 62 years. African-Americans have a propensity to show pathology at younger ages(3,10).

Unstable angina is caused by obstacles in the blood flow that generate a lack of perfusion in the myocardium. The initial perfusion starts directly from the heart towards the aorta and subsequently in the direction of the coronary arteries, which supply their respective parts of the heart. The left coronary artery branches into the circumflex artery and the left anterior descending artery. Subsequently, they branch into smaller vessels. The right coronary artery also has smaller branches. Unstable angina occurs when blood flow to the myocardium is impeded. Typically, this blockage may be caused by intraluminal plaque formation, intraluminal thrombosis, vasospasm, and elevated blood pressure. Usually, a mixture of these is the precipitating factor(3,11).
Factors that increase myocardial oxygen demand:

- AV shunts.
- Arrhythmias.
- Fever.
- Hypertension.
- Anemia.
- Thyrotoxicosis.
- Aortic stenosis.
- Pheochromocytoma.
- CHF.
- Cocaine use.

Anamnesis and Physical Examination
Affected individuals usually show chest pain and shortness of breath. Chest pain will usually be reported as a pressure type, however it does not necessarily present with this description. They may present with squeezing, burning, and sharp types of pain. Often the pain radiates to the jaw or arms, occurring on both the left and right sides. Other symptoms that may occur are nausea, diaphoresis, dizziness, vomiting and palpitations. Exertion may aggravate the pain and rest may decrease it. The use of nitroglycerin and aspirin may improve the pain. A characteristic factor of unstable angina is that the pain may not be fully restored with these reported relieving factors. In addition, several individuals present with coronary artery disease. This may denote established coronary artery disease or symptoms that they have been experiencing for a certain period of time.

These individuals may be accustomed to the symptoms and may report an increase in episodes of chest pain that will take longer to resolve, as well as an increase in the seriousness of the symptoms. These symptoms show that unstable angina is the most likely diagnosis, as opposed to stable angina or other causes of chest pain. It is vital to keep this in mind, because these differences may suggest impending myocardial infarction, ST-segment elevation myocardial infarction (STEMI), and should be assessed as soon as possible because of the risk of morbidity and mortality(3,12).

The examination is likely to be normal, however the patient may be chest tightening, shortness of breath, diaphoresis, tachycardic heart sounds and sometimes rales due to pulmonary edema.
Findings suggestive of a high-risk situation are:

- Presence of rales and crackles.
- Hypotension.
- Dyskinetic apex.
- Elevated JVP.
- Presence of S3 or S4.
- New apical systolic murmur.

Evaluation
When a patient presents with symptoms suggestive of angina, he/she should be evaluated promptly and an ECG should be performed to assess for ischemic signs or possible STEMI. The ECG in unstable angina may show hyperacute T waves, flattened T waves, inverted T waves and ST segment depression. ST elevations indicate STEMI and these individuals should be managed with percutaneous coronary intervention or thrombolytics pending availability of catheterization. Acute coronary syndrome may be accompanied by any number of arrhythmias, including junctional rhythms, ventricular fibrillation, left bundle branch block, sinus tachycardia, ventricular tachycardia, and others. Most commonly, however, the individual is in sinus rhythm, primarily in the case of unstable angina rather than infarcted tissue.

The individual should have laboratory tests that include a complete blood count to evaluate anemia, platelet count and a basic metabolic profile to screen for electrolyte abnormalities. In addition it is advisable to perform fasting blood glucose, glycated hemoglobin (HbA1c) and thyroid stimulating hormone (TSH). A troponin test should be ordered to find out if any myocardial site has developed an infarction. A pro-brain natriuretic peptide (Pro-BNP) may be checked, because a higher level is associated with a higher risk of mortality. Coagulogram should be used if the affected individual will be anticoagulated or if anticoagulation is anticipated. Usually, a chest X-ray will present the size of the heart and mediastinum allowing to detect dissection, as well as other explanations of precordial pain.

It is important to stress the history to detect other possible emergent origins of chest pain, shortness of breath, pulmonary embolism, pneumonia, pneumothorax, aortic dissection, and esophageal rupture. The individual with angina should remain on a cardiac monitor to watch for any rhythm changes. Occasionally additional tests such as cardiac stress tests, treadmill stress test, myocardial perfusion imaging, cardiac CT/MRI or the gold standard, stress echocardiogram and cardiac catheterization may be performed. Typically, these are ordered and performed by

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hospital care providers as well as primary care providers, however, with the rise of observational medicine, emergency medicine providers may request them(3,6,13).

Echocardiogram: allows assessment of ventricular function, as well as analysis of the contractility of the various segments. The presence of akinesia or hypokinesia in segments supplied by a coronary artery strongly suggests coronary artery disease. The echocardiogram also rules out some other origins of chest pain, such as valvular problems.

Chest X-ray: serves to rule out secondary causes of pulmonary origin, such as pleural effusion. In order to select the most appropriate complementary examination, it is important to know the probability that the affected individual is suffering from coronary artery disease(14).
Assessment of the risk of acute coronary syndrome:

- ST depression or elevation greater than 1 mm.
- Marked symmetrical T wave inversion.
- Previous MI or known history of CAD.
- Transient ECG or hemodynamic changes during chest pain.
- Chest, neck or left arm with documented angina.

Treatment
The basis of treatment focuses on improving perfusion of the coronary arteries. This is done in multiple ways.

Affected individuals can be managed with aspirin as antiplatelet therapy, 162 to 325 mg orally or 300 mg rectally, if the individual is unable to swallow. Aspirin should be given within 30 minutes. Clopidogrel is an alternative for aspirin intolerant individuals. Prasugrel is more effective than clopidogrel, however it is associated with a higher risk of bleeding. Ticagrelor is currently approved, in addition to aspirin, to decrease the rate of thrombotic cardiac events.

Nitroglycerin comes in multiple presentations, intravenous, sublingual, transdermal and oral, it improves perfusion through vasodilation of the coronary arteries, which allows optimizing blood flow and blood pressure. This will reduce the amount of work the heart must do, which reduces the heart's energy demand.

Supplemental oxygen should be administered through a nasal cannula to maintain correct oxygen saturation. These 3 actions are the most rapid and essential functions to perform in the assessment and treatment of unstable angina. In individuals with ongoing pain or longer recovery time, the response of the affected individual should be assessed because of a greater risk of myocardial infarction.

Other potential therapies include anticoagulation with high or low molecular weight heparin. Beta-blockers can also reduce energy demand by lowering blood pressure and heart rate. One drug ranolazine used in individuals with unstable angina showed a significant decrease in the endpoint of recurrent ischemia. Several studies have validated the use of statins in individuals with unstable angina(3,15).
Diabetes is an independent predictor of adverse outcomes in individuals with medically managed unstable angina(16).
Cardiac angiography is indicated in unstable angina if the affected individual presents:

- Cardiogenic shock.
- Depressed ejection fraction.
- Angina refractory to pharmacological treatment.
- Unstable arrhythmias.
- Early PCI in NSTEMI (within the first 6 hours) has been shown to have lower mortality compared to those undergoing late PCI.

Differential Diagnosis
The differential diagnosis of angina can be classified according to body systems:

- Gastrointestinal: hiatal hernia, gastroesophageal reflux, peptic ulcer.
- Pulmonary: pneumothorax, pulmonary embolism, pneumonia.
- Musculoskeletal: muscle spasm, costochondritis, rib injury, chest wall injury.
- Psychiatric: panic attack, generalized anxiety.
- Non-ischemic cardiac: pericarditis, myocarditis.
- Vascular: aortic dissection(1).

In the specific differential diagnosis of unstable angina we have:

- Aortic dissection.
- Pulmonary embolism.
- Peptic ulcer disease.
- Pericarditis.
- Pneumothorax.
- Essential complications of unstable angina include:
- Myocardial infarction.
- Stroke.
- Death(3).

There is evidence showing that individuals with recent ST-segment elevation (more than 1 mm) have a 12-month MI or death rate of about 11%, compared to only 7% of individuals with only isolated T-wave inversion.
Negative prognostic factors include:

- Hemodynamic instability.
- Continuous congestive heart failure (CHF).
- Sustained VT.
- Recurrent episodes of angina despite maximal treatment.
- Low ejection fraction.
- New or worsening MR.

Prevention
The objectives of prevention are to enable the affected individual to return to all activities of daily living, in addition to preserving myocardial function and preventing future cardiac events. Currently, most cardiac centers have specialized teams, such as

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cardiac rehabilitation, providing intensive and effective counseling.

- Lifestyle: smoking cessation is mandatory to prevent repeated cardiac events. Lipid-lowering individuals should aim for a target LDL-C level of 70 mg/dl or less, an HDL level of at least 35 mg/dl and a triglyceride level of less than 200 mg/dl. The affected individual should be physically active and have a low-fat diet.
- Control of hypertension: with the objective of maintaining blood pressure below 140/90 mm Hg, as well as reducing sodium and alcohol intake.
- Management of diabetes mellitus: blood sugar levels can be reduced with diet, physical activity or drug therapy.
- Weight control and nutritional counseling: the patient should be guided to lose weight and achieve an appropriate body mass index (BMI).
- Activity management: individuals at risk for unstable angina should avoid strenuous physical activity, particularly in cold weather.

CONCLUSIONS

Unstable angina is characterized by an onset during rest, its diagnosis is clinical so it is of vital importance to know its clinical and epidemiological manifestations and its evaluation to reach a correct diagnosis, in order to ensure timely and adequate treatment. Since this condition continues to be a public health problem that affects a high percentage of the population on a daily basis, awareness of the problem should be raised, in addition to trying to prevent it by modifying lifestyle.

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Conflict of Interest Statement

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