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Review article

CURRENT PHARMACOLOGICAL AND NON-PHARMACOLOGICAL TREATMENT APPROACHES IN CONGESTIVE HEART FAILURE.

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ABSTRACT

Patients older than 65 years old have congestive heart failure at a higher rate than any other condition that leads to hospitalisation. There are almost 700,000 new cases of heart failure diagnosed each year, and re-hospitalization rates can reach as high as fifty percent within the first few months after an individual has been initially discharged from the hospital. It is essential for the management of congestive heart failure to have a solid understanding of the therapeutic drugs that not only help reduce the rates of mortality and morbidity, but also reduce the number of times patients need to be readmitted. In this section, the writers discuss the many different categories of medications that are utilised in the treatment of heart failure. They then proceed to present a focused review that examines the several clinical trials that have prioritised the study of mortality, morbidity, and hospitalisation rates in heart failure patients who are receiving the various types of treatment medicines.

Key Words:- ACE Inhibitors, Ionotrope, Congestive Heart Failure, Beta-Blockers.

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INTRODUCTION

Heart failure, often known as HF, is a collection of clinical symptoms and signs that are brought on by abnormalities of the heart's structure and/or function [Hashem *et al*., 2017]. The ensuing treatment is determined by the specific pathology that is behind it. The term "heart failure with mid-range ejection fraction" has been replaced with "heart failure with mildly reduced ejection fraction" in the most recent guidelines published by the European Society of Cardiology (ESC). These guidelines have also been revised and structured according to the current classification of different types of heart failure (HFmrEF) [Starling Rc, 2016][Potter *et al*.,2006].

The medical term for this condition is congestive heart failure (CHF), and it occurs when the heart is unable to pump blood at a rate that is sufficient to fulfil the oxygen demands of the rest of the body. In addition to being brought on by cardiac failure, it can also be brought on by situations characterised by both high demand and high production. Despite the many compensating mechanisms that take place within the body, poor blood circulation is the result of a heart that is failing to function properly. These mechanisms include an increase in blood volume, an increase in cardiac filling pressure, an increase in heart rate, and an expanded cardiac mass as a result of the rise in heart rate. In spite of these modifications, the heart will typically continue to lose its capacity to contract and relax in a suitable and adequate manner, which will ultimately lead to chronic heart failure [Packer *et al*., 2017].

The treatment that is necessary for heart failure can range from nonpharmacologic to pharmacologic approaches, and it also includes the use of invasive therapies when necessary. The non-pharmacologic treatment includes limiting sodium and fluid intake, engaging in appropriate physical activity, and monitoring and managing weight gain. Angiotensin-converting enzyme (ACE) inhibitors (ACEi), aldosterone receptor blockers (ARB), vasodilators, beta-blockers (BB), aldosterone antagonists and inotropic drugs. together with diuretics and anticoagulants, are all components of pharmacologic therapy. In the meantime, invasive therapies include cardiac resynchronization therapy, implanted cardioverter-defibrillators, and pacemakers. In addition to medical treatment, surgical procedures, such as coronary artery bypass grafting and heart transplants, are sometimes utilised in the treatment of heart failure.

New 2012 guidelines for all NYHA classes of heart failure include the use of an ACEi in addition to a BB for all patients with an ejection fraction (EF) less than 40 percent in an effort to lower the likelihood of hospitalisation due to heart failure. Patients with persistent symptoms and an EF less than 35% despite treatment with a BB and an ACEi or an ARB may also consider adding an aldosterone antagonist to their management regimen [Sato *et al*., 2017].

SIGNS AND SYMPTOMS:

Dyspnea is the most prevalent symptom that emergency department patients present with when they have ADHF, regardless of the underlying aetiology. Orthopnea, paroxysmal nocturnal dyspnea, poor exercise tolerance, peripheral edoema, weakness, and weariness are some additional symptoms that may be present. Patients diagnosed with ADHF may present with either hypertension or hypotension, depending on the classification of the condition and the underlying reason. In spite of the fact that the vast majority of patients exhibit tachycardia, bradycardia may be present in situations where the patient is experiencing toxicity from medication (such as b-blockers or digoxin) or high-degree atrioventricular block. Patients who have ADHF may have pulmonary edoema, peripheral edoema, jugular venous distention, hepatomegaly, hepatojugular reflux, and a third heart sound when they have a physical examination.

DIAGNOSIS:

ECG, CXR, bedside echocardiography, and laboratory analysis are commonly used in the diagnostic examination of a patient with suspected ADHF.

CLASSIFICATION:

Clinical syndromes have been defined by the European Society of Cardiology for the treatment of acute coronary syndromes. Some patients have overlapping symptoms, but their proper classification is critical because everyone requires a unique therapy approach.

Classification of acute heart failure:

1. Acute decompensated heart failure (ADHF).
2. Hypertensive acute heart failure
3. Pulmonary edema
4. Cardiogenic shock
5. Right heart failure
6. Acute coronary syndrome complicated by acute heart failure

NON-PHARMACOLOGICAL APPROACHES:

Patients with an EF of less than 30 percent and NYHA classes I, II, or III with a life expectancy greater than six months are candidates for insertion of an intracardiac device (ICD). Specifically, it has been demonstrated that NYHA class IV patients do not benefit from ICD implantation, whereas class II patients gain the most in terms of reductions in sudden death and mortality relative to other heart failure patients. Multiple studies have examined the impact of ICDs on heart failure patients in greater detail. The DE Fibrillators In Non-Ischemic cardiomyopathy Treatment Evaluation (DEFINITE) study recruited 458 patients with dilated non-ischemic cardiomyopathy with an EF of less than 36%. Patients on regular medical care were compared to patients on standard medical therapy with a single-chamber ICD. In the ICD arm of the research, there were only 28 deaths at follow-up, compared to 40 deaths in the normal medical care arm. Moreover, there were only three sudden deaths in the ICD group compared to fourteen in the medical therapy group. The Multicenter Automatic Defibrillator Implantation Trial (MADIT) II trial examined the effects of ICDs in patients having a history of MI and an EF of less than 30%. This study examined 1232 patients and found that the combination of ICD implantation and pharmacological therapy reduced death by 28% over a three-year period. The Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) was a larger study that involved 2521 patients with NYHA class II or III heart failure symptoms and an EF of less than 35%. Three groups were examined: conventional therapy plus placebo, conventional therapy plus amiodarone, and conventional therapy plus an implantable cardioverter defibrillator (ICD). At the initial follow-up point of 45.5 months, the ICD arm had the lowest mortality rate, at 22%, and a 23% lower risk of death compared to the placebo arm [Tariq and Aronow, 2015] [Armstrong *et al., 2020*].

PHARMACOLOGICAL APPROACH:

Preload and afterload are the primary targets of pharmacologic therapy in patients with ADHF. When preload is decreased, so is myocardial wall strain and

oxygen demand in the heart. The left ventricle's myocardial work is reduced when afterload is reduced, which increases cardiac output and perfusion of tissues. nitrates, angiotensin-converting enzyme (ACE) inhibitors, diuretics, and inotropes are common groups of drugs used to treat ED patients with ADHF [Teerlink *et al.*,2021].

The first line of treatment for ADHF sufferers is nitroglycerin, a nitrate. Nitroglycerin decreases preload primarily via diluting the venous system at low doses. Nitroglycerin produces arterial dilatation and, as a result, a reduction in afterload at larger doses. While suitable intravenous access is being established, nitroglycerin can be administered sublingually (400 mg every 5 minutes). A nitroglycerin infusion should begin as soon as the patient has been able to gain access. Depending on the institution's requirements, the infusion may begin at 20 mg/min. The speed at which the infusion is titrated to achieve clinical improvement is vital for the emergency physician. Up to a dose of 200 mg/min, the rate of nitroglycerin infusion can be raised by 40 mg/min increments every five minutes. When nitroglycerin infusions were started at larger doses than the standard 20 mg/min, recent trials showed lower intubation rates without hypotension. The safety and efficacy of this method need to be proven in larger research [Mc Donagh TA *et al.,2021*].

Patients unresponsive to nitroglycerin and those with severe hypertension may benefit from additional afterload reduction with sodium nitroprusside. The initial intravenous dose of nitroprusside is between 0.100 and 0.125 mg/kg per minute. The rate of infusion can be increased by 0.1 mg/kg per minute every 5 minutes, up to a maximum of 400 mg/min. Significantly, nitroprusside is converted to cyanide, which can rapidly accumulate in people with renal failure. Moreover, nitroprusside may increase mortality in patients with acute myocardial infarction [Benjamin *et al.*, 2017].

ACE inhibitors are helpful at reducing afterload and have been used to treat patients with ADHF in the emergency department. Multiple small-scale investigations on ACE medications in patients with ADHF have showed an improvement in hemodynamic indicators. In addition, a single-center trial revealed that patients who received sublingual captopril as part of their ED treatment had lower rates of intubation and admission to the intensive care unit. Importantly, the American College of Emergency Physicians' current guidelines include ACE inhibitors among the therapeutic alternatives for ED patients. Enalaprilat and captopril are the most widely utilised ACE inhibitors in investigations of people with ADHF. Enalaprilat can be taken intravenously at a dose of 1.25 mg over 5 minutes, while captopril can be given intravenously or sublingually [Moreno Aliaga *et al.*, 2011].

Historically, diuretic medicines have been regarded as the cornerstone of pharmacologic treatment for ADHF. Since the majority of ED patients with ADHF who are acutely unwell are not volume overloaded, the indiscriminate administration of diuretics could be detrimental. These drugs require adequate renal perfusion to be effective. Consequently, diuretics play a limited role in the emergency department care of patients with ADHF. The use of a diuretic should not supplant established therapies, such as NPPV and nitrates. When a diuretic is deemed necessary, furosemide is most frequently prescribed. Patients who do not typically take furosemide as an outpatient can receive an initial dose of 20 to 40 mg. Patients who have already been prescribed furosemide can receive an initial intravenous dose equivalent to their oral outpatient dose. Studies comparing high-dose and low-dose diuretic therapy, as well as those comparing intermittent bolus doses with continuous infusions, have not shown superior outcomes with any dose or strategy [Obana *et al.*, 2010].

Patients with ADHF who exhibit indications of cardiogenic shock should be evaluated for inotropic treatment. Emergency physician-performed bedside echocardiogram can be incredibly helpful in identifying patients who may benefit from inotropic assistance. Current guidelines propose commencing inotropic drugs after optimising nitrate and diuretic therapy. Dobutamine and milrinone are the most frequently prescribed inotropic drugs for these patients. A dobutamine infusion can be commenced at a rate of 2.5 mg/kg per minute and increased by 2.5 mg/kg per minute every 10 minutes up to a maximum rate of 20 mg/kg per minute. Mechanism and duration of action are significantly distinct between these two drugs. Although dobutamine activates adrenergic receptors, enhanced contractility and decreased afterload ensue. Milrinone inhibits phosphodiesterase; as a result, an increase in cyclic adenosine monophosphate results in greater contractility and diastolic relaxation, as well as vasodilation and, thus, lower afterload. Because it does not rely on sympathetic receptors, chronic b-blocker therapy patients may prefer it. Milrinone has more potent vasodilatory effects than dobutamine, making it preferable for individuals with severe pulmonary hypertension. Importantly, the half-life of milrinone is between 2 and 4 hours, but that of dobutamine is only 2 minutes. If the patient's blood pressure remains insufficient despite inotropic therapy, a vasopressor (such as norepinephrine or epinephrine) may be administered. It is essential to remember that inotropic drugs can have serious adverse effects such as hypotension and tachydysrhythmias [Van der Meer *et al.*, 2019]. Therefore, they should not be routinely administered to all patients with ADHF. In fact, a number of studies indicate that the mortality rate rises when these drugs are used extensively.

CONCLUSION:

Patients diagnosed with ADHF who present to the emergency department (ED) are typically in a critical condition and require prompt medical attention. Many of them, in contrast to the conventional method of instruction, do not have an excessive amount of information. Rapid beginning of NPPV treatment in conjunction with aggressive nitrate titration is the cornerstone of emergency department (ED) management of patients diagnosed with ADHF. Afterload reduction with an ACE inhibitor is an option that might be examined for people who do not react to increasing their doses of nitrates. It is not recommended to deliver a diuretic before these essential actions have been finished, but it is OK to do so if the preload and afterload have been successfully reduced to their ideal levels. There are certain patients with cardiogenic shock and ADHF who, while receiving normal treatment, may benefit from receiving inotropic therapy for a shorter period of time.

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