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Review Article **Dentistry**

Enalapril and Nifedipine Effects on NIDDM Cardiac Patients: A Review

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Abstract

Cardiovascular diseases (CVDs) are common in patients with Non-insulin-dependent diabetes mellitus (NIDDM). Lack of exercise and obesity in the population; the main causes of T2D prevalence. Therefore there is a need for joint treatment of diabetes and CVDs. Calcium-channel-blocking drugs and angiotensin-converting–enzyme (ACE) inhibitors are considered very effective. Angiotensin-converting–enzyme (ACE) inhibitors are thought to be very efficient in reducing the risk of death and hospitalization in patients with HF (heart failure). These inhibitors act as potential regulators of insulin and cardiac failure. This review article focused on the mechanism of action of two the action of drugs, Enalapril (angiotensin-converting–enzyme (ACE) inhibitors) and nifedipine (Calcium-channel-blocker), and their clinical effect on reducing the CVDs and heart failure in T2DM patients. Furthermore, novel immuno targets are needed to discover in future that may lower the risk of deaths among diabetes patients.

Keywords: NIDDM, Calcium-channel blockers, heart failure, cardiovascular diseases.

INTRODUCTION

Diabetes mellitus is a metabolic disease that increased the prevalence rate in adults from about 4.7% in 1980 to 8.5% in 2014. Noninsulin-dependent diabetes mellitus (NIDDM) also known as Type 2 diabetes (T2D), is common in adults and 90–95% of diabetic patients have T2D. The prevalence rate of T2D is much higher in children and adolescents. Lack of exercise and obesity in the population is the main cause of T2D prevalence [1].

In developed countries like the United States, there is a high risk of T2D as an estimated 12.2% or 30.2 million adults had diabetes in 2015, of which 23.3 % (7.2 million) were not well aware of common symptoms leading to the cause of diabetes [2]. Type 1 and type 2 diabetes are heterogeneous in nature that varies based on clinical symptoms and treatment. Type 2 diabetes has a high chance with 90-95% mostly in age more than 40 years old [3].

Different factors are involved in the progression of T2D and most of them are inflammation indicators and accidental events. The main factors for death in Type 2 diabetes patients are cardiovascular diseases (CVDs), majorly heart failure (HF), coronary artery disease (CAD), and stroke [4, 5] .It has been observed that cardiac infarction is also contributing to T2M and is needed for bed rest and appropriate medications [6] .

A large number of cases were reported in the last few years. In 2012, 1.5 million deaths occurred due to diabetes and caused an additional 2.2 million deaths due to unregulated monitoring of the high sugar level [1]. Most of them, 43% of these 3.7 million deaths were common in the 70, and most were unable to survive due to heart failure. Patients with diabetes have a 2-3 times high risk of CVD than those without diabetes [7].

Diabetes mellitus also caused an increase in blood pressure (Hypertension) and chances become so high at age more than 30 and it is a great risk for CVD (cardiovascular disease) [8]. T2DM patients have high chances of cardiac failure as blood sugar is mostly high that disrupted the heart functions and damages the heart walls [9]. The main factors contributing to the increased risk in T2DM patients are hypertension, CAD (coronary artery disease), and hypercholesterolemia.

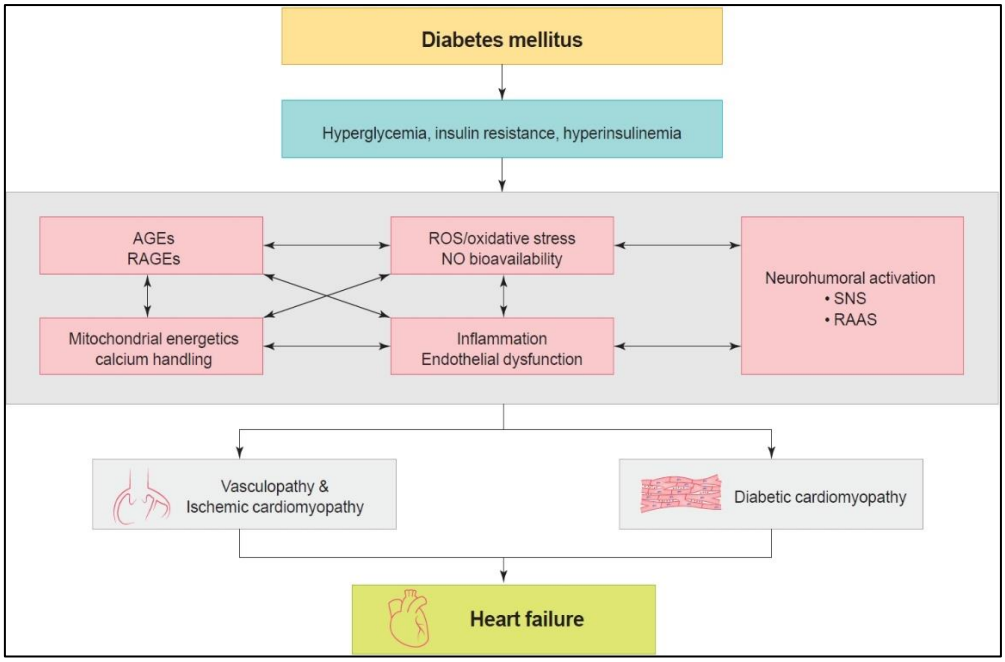

Figure 1: Showss the heart failure in diabetic patients [28]

Management of Cardiovascular disease in NIDDM/ T2DM

Due to the increased rate of cardiovascular diseases (CVDs) in Type 2 diabetes patients, the awareness related to the joint management of CVD and T2DM has increased [9-10]. The expenditures and costs of medication observed for diabetes exceed 827 billion US dollars worldwide [11]. Due to the non-functionality of medical instruments, losses will increases by 2030 due to diabetes will total 1.7 trillion US dollars with 800 billion US dollars for low- and middle- income countries and 900 billion dollars for high-income countries [1]. Improving the lifestyle and weight balance may maintain the insulin balance in diabetes and decrease the risk of cardiac diseases. 5% weight loss is linked to high levels of HDL cholesterol, and a decrease in triglycerides in patients with diabetes [12].

Angiotensin-converting–enzyme (ACE) inhibitors are thought to be very efficient in reducing the risk of death and hospitalization in patients with HF (heart failure). These inhibitors act as potential regulators of insulin and cardiac failure [13-14]. Calcium-channel–blockers may eradicate the number of risks including disease pulmonary hypertension, cardiac arrhythmias, and Raynaud's phenomenon that lead to cardiovascular diseases [15].

Role of Enalapril and Nifedipine

Enalapril, an Angiotensin-converting–enzyme (ACE) inhibitor is very effective in decreasing the risk of hospitalization and death in patients with heart failure. Similarly, Nifedipine which is a calcium channel blocker is extensively used for the treatment of hypertension which is the main cause of cardiovascular disease [16].

Table 1: Shows the role of Enalapril and Nifedipine and associated risk factors

Disease Type/Treatment Indications	Risk Factor	Metabolism Interface/Function	Other Complications	References
Cardiovascular Diseases	Non-insulin-dependent diabetes mellitus (NIDDM)	Insulin	Heart Failure, dizziness,	[2-6]
Enalapril	These inhibitors are act as potential regulators of insulin among patients with NIDDM	Cardiac failure and reducing the	Dizziness from blood pressure, Headaches. Loss of taste.	[16-21]
Nifedipine	Reduced the stroke and peripheral revascularization	Lowering the risks of myocardial infarction,	Muscle cramp, headache	[25]

It has been reported that both drugs (enalapril and nifedipine) lowered blood pressure effectively. When these two drugs were applied to different groups of patients with type T2DM, it has been found that after 6 months of follow up systolic blood pressure (SBP) and diastolic blood pressure (DBP) was higher significantly (P_0.01) in the enalapril group as compared to nifedipine group. In the same study,

nifedipine caused 33 adverse reactions related to the vasodilatory effect while 34 adverse effects (cough accounted for 25/34) were caused by enalapril [17]. When enalapril was given in comparison with the sacubitril/valsartan combination, it was observed that the risk for death and HHF (hospitalization for heart failure) in patients with HFrEF (HF with reduced ejection fraction) was decreased in sacubitril/valsartan group than ACE-inhibitor (enalapril) [18].

A study carried out including 470 patients who had hypertension showed the same control of blood glucose, blood pressure, lipid concentration, and smoking behavior in the enalapril group (235 patients) as well as in the nisoldipine group (235 patients) group after a follow-up of five years [19].

The efficacy of the Angiotensin-converting–enzyme inhibitor (enalapril) for the prevention of cardiovascular disease showed that men who received enalapril had fewer CV events than those who were on a thiazide diuretic. While the same number of CV events were observed in women who were treated with enalapril or diuretic [20].

Enalapril was given randomly in comparison to Placebo in CONSENSUS (Cooperative North Scandinavian Enalapril Survival Study). After 188 days of follow-up the death rate was 44% in the placebo group while in the enalapril group, it is 26% [21].

Similar treatments (enalapril or placebo) were given to the heart failure patients In the SOLVD Treatment trial. After the follow-up of 41 months on average, a 16% death rate was found in enalapril while this rate is 40% in the placebo group. It has been reported in The SOLVD-Prevention trial that the risk of heart failure was reduced by enalapril.The use of the Angiotensin-converting–enzyme (ACE) reduced the risk of death and HF hospitalization [22-24].

A 13% reduction in myocardial infarction, stroke and peripheral revascularization, heart failure, and refractory angina by nifedipine (Calcium-channel-blocker) has been reported in the hypertensive group when compared to the normotensive. Nifedipine also reduced the need for coronary angiography by 16% in hypertensives and 21% in normotensives. It also decreased stroke incidence in both subgroups by 30% [25]. Due to having anti-oxidant properties, nifedipine inhibits glycoxidation and glycation. So, it could constrain vascular calcification by restricting the AGE formation in diabetic patients. In addition to anti-hypertensive action, the long-acting nifedipine may have a favorable antiatherosclerotic effect in T2DM patients [26-28].

CONCLUSION

Diabetes mellitus is metabolic disease and several complications are associated with disease progression such as cardiovascular diseases, liver failure and heart failure. Metformin is the ideal medication that showed promising results against type 2 diabetes. Its function directly regulation of glucose production in the liver and improving body sensitivity to insulin. Furthermore, novel immuno targets are needed to discover in future that may lower the risk of deaths among diabetes patients.

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