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The Effect of Rennin-Angiotensin Blockers on Ejection Fraction in Patients with Left Ventricular Systolic Dysfunction Heart Failure

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Abstract:

Introduction: Left ventricular systolic dysfunction (LVSD) is a type of heart failure characterized by low ejection fraction (EF) and increase in mortality and morbidity. Rennin- Angiotensin Blockers are confirmed to improve EF and quality of life in patients with LVSD.

Objective: The aim of this study was to assess and compare the effect of rennin angiotensin blockers on EF in patient with LVSD.

Methodology:80 patients with LVSD were assigned to use either ACEI (lisinopril) or ARBS (losartan or candesartan); patient's clinical data and Echocardiography had been followed for 6 months.

Results: There was improvement on EF; by 9% in the group taking ACEI (lisinopril) and by 8% in the group taking ARBS. 52.6% of patients showed improvement in their QOL.

Conclusion: There is an improvement on the EF% in the ARBS (losartan or candesartan) group as well as the ACEI (lisinopril) group. There was no significant difference when comparing the effect of the 2 groups of drugs on the EF%. The quality of life improved in most patients with treatment with these drugs.

Key wards: Left ventricular systolic dysfunction, ejection fraction, Rennin-Angiotensin Blockers.

Introduction:

Heart failure (HF) is a life-threatening condition in which the heart can no longer pump enough blood to the body.(1) Left side heart failure is a type of HF characterized by left ventricular systolic dysfunction (LVSD) and a subset of symptoms, including fatigue, cough and shortness of breath due to pulmonary congestion .(2) Ischemia is by far the commonest cause of LVSD.(3) According to the New York Heart Association (NYHA), heart failure can be classified into four levels, Class Ⅰ: Asymptomatic left ventricular dysfunction, class Ⅱ: Mild heart failure, class Ⅲ: Moderate heart failure, class Ⅳ: Severe heart failure. In systolic dysfunction, the left ventricular ejection fraction (LVEF) is <40% and may even be <20%.Thus systolic function is almost matching with ejection fraction (2). Quality of life is adversely affected by functional inability. Of high consequence is the high mortality rate. Among those with severe HF, 30 to 50% will die within 1 year and 70 % within 3 years. In the Framingham study, 5 year survival

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rates are lower in men (38%) than in women (57%). In spite of earlier diagnosis and proper medical management, the prognosis is poor. Only with the introduction of vasodilator and angiotesin converting enzyme inhibitor (ACEI) (lisinopril) and angiotesin receptor blockers (ARBS) (losartan or candesartan) therapy had mortality been decreased. [2] ACEI (lisinopril) inhibitors are indicated as first-line treatment for all grades of heart failure due to LVSD, including calss Ⅰ NYHA. They exert their effects by reducing both preload and after load on the heart thereby improving cardiac output. ACE inhibitors act upon the rennin angiotensin-aldesterone system, and they reduce after load by reducing the generation of angiotensin II. Which is a potent vasoconstrictor. [2] ACEI (lisinopril) inhibitors are well tolerated by most patients and have been shown to improve the quality of life and survival in patients with mild to severe systolic dysfunction. [1] It should be noted, however, that Maximal ACEI (lisinopril) inhibition does not completely suppress angiotensin II formation, as non–ACE-mediated pathways still allow its formation via proteases such as chymase, cathepsin G, and tissue plasminogen activator.[4] These factors all contribute to the concept of "angiotensin II reactivation". Orally active angitensin type I receptor antagonists, such as losartan, represents.NPew agents that offer an alternative method of blocking the rennin angiotensin system. [4]

Many major clinical trials on blocking the rennin-angiotensin systems are well known, Inconsnsus trial the aim was to determine how the ACEI (lisinopril) inhibitor enalapril had an impact on the prognosis of severe heart failure patients. [5] The SOLVD trial designed to study the effect of an angiotensin-converting-enzyme inhibitor, enalapril, on mortality and hospitalization in patients with chronic heart failure and ejection fractions less than or equal to 0.35. [6] Effects of candesartan (ARBS)(losartan or candesartan) in patients with chronic heart failure and reduced left-ventricular systolic function were studied in CHARM Program [7]. ELITEII Losartan heart failure survival study had been done to confirm whether losartan is superior to captopril in improving survival and is better tolerated. [11] The main objective of this study was to compare between Rennin-Angiotensin Blockers in patients with Left Ventricular Systolic Dysfunction heart failure in term on their effect on ejection fraction and Quality of life.

Methodology:

This prospective study was conducted at AL-shaab Teaching Hospital and Sudan Heart Center in Khartoum Sudan, where 80 patients with left ventricular systolic dysfunction (LVSD) had responded. It was initiated in April 2015 and was completed in October 2015. The diagnosis of LVSD was established with proper medical history and clinical examination. ECG, CXR and Echocardiography were used to confirm the diagnosis and for follow-up during the study period. After confirming their consent to participate in the study verbally, patients were assigned to use either ACEI (lisinopril) or ARBS (losartan or candesartan). Starting dose of lisinopril was 2.5 mg once daily which was up titrated each two weeks until reaching target dose of 20 mg once daily or maximum tolerated dose. Losartan group patient started by 12.5mg once daily and up titrated to

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50mg once daily according to patient tolerability and patient taking candesartan started with 4mg once daily and dose increased at interval at least 2 weeks until a target dose of 32mg once daily was reached according to clinical response. Patient echocardiography was followed up during the 6 months with regard to EF% improvement, the Echocardiography being done by the same operator.

Patient's quality of life was followed up during the 6 months of treatment using the Minnesota living with heart failure questionnaire. Patients underwent renal function tests for safety monitoring before initiation of treatment and during dose titration.

Results:

Out of 80 patients who responded 53(66.3%) of them were males and 27 (33.7%) of them were females. The mean age was 55 years. All patients were diagnosed as LVSD heart failure NYHA class Ⅱ- Ⅳ. Of the total respondents included in the study 46(57.5%) patients received ACEI (lisinopril) and the rest 34(42.5%) received ARBS (losartan or candesartan) . Table (1) shows the mean and standard deviation of EF% of patients taking ACEI (lisinopril) and ARBS (losartan or candesartan) during the 6 months of treatment which shows improvement by 9% within ACEI (lisinopril) group and by 8% of ARBS (losartan or candesartan) group. There is significant improvement in the EF% during the treatment with ACEI (lisinopril) and ARBS (losartan or candesartan) group whereas, both groups were well matching and consistent as shown in Table (2).

It was found that there was no significant difference between the 2 groups of drugs, with regard to their effect on EF% (pr: 0.809 and 0.305). The impact of both drugs on the quality of life during 6 months of treatment is shown in Table (3). However, ARBS (losartan or candesartan) were found to have slightly better effect on quality of life than ACEI (lisinopril).

Table (1): The mean and standard deviation of EF% of patient taking ACEI and ARBS during the 6 month of treatment:

	Drug	Mean	Std. Deviation	Std.Error Mean
Ef1*	ACEI	24.7826	6.53168	.96304
	ARBs	24.8235	5.49639	.94262
Ef3*	ACEI	33.9783	7.01265	1.03396
	ARBs	32.7647	6.19413	1.06228

*Ejection fraction (readings 1 and 3).

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Table (2):Significant improvement in the EF% during the treatment with ACEI and ARBS.:

	N	Correlation	Sig.(PValue)
PairEf1&Ef3(ACEI)	46	0.898	0.001
Pair EEf3(ARBS)	34	0.829	0.002

Table (3):Impact of ACEI and ARBS on QOL

Degree	No. of patients	Percent
Excellent	3	3.8
Good	39	48.8
Reasonable	29	36.3
No change	7	8.8
Deteriorate	2	2.5
Total	80	100

Discussion:

The patients in this study ranged from those stable, attending the outpatient clinic to those on the ward being treated for severe heart failure. All of them receiving the conventional treatment with loop diuretics and ACEI(lisinopril) inhibitors. The follow up of our study was six month, the mean of LVEF was 24.78%, and the mean age was of 55 years .The number of male patients was 53 and the females was 27 which is almost half the number of male patients, this was consistent with the previous trial (female gender under –represented).[8] Our statistical findings showed an improvement in the EF% by 9% for the ACEI (lisinopril)group after 6 months duration of treatment while in the group of ARBS (losartan or candesartan) the improvement was by 8% after the same period. This improvement was found to be significant for the groups of patients (p=0.001 for the ACEI (lisinopril) group=0.002 for the ARB (losartan or candesartan) S group), regardless whether they reached the target dose or not. These findings were the same as found in landmark trials which shows an increase in EF from 21% to 30 %(9%) in 6 months (p<0.001). [14] On the other hand when comparing the effect of the ACEI (lisinopril) and ARBS (losartan or candesartan) on EF there was no significant differences between the 2 groups of drugs (P Value was= 0.809 and 0.305 respectively). This is similar to the ELITE Ⅱ trail. [11] Quality of life is adversely affected by

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progression of functional disability, and of great consequence is the high mortality rate. Despite earlier diagnosis and aggressive medical management, the prognosis is poor. Only with the advent of vasodilator and angiotensin converting enzyme inhibitor therapy has mortality been reduced. (1) It was found that After 6 month's therapy administered to total of 80 patients, their quality of life varied accordingly to their susceptibility to the drugs (ACEI/ARBS). In general terms, the quality of life improved in most patients over the time, however 2.5% of them complained of a deteriorated life style, 8.8% claimed that their quality of living was not changed after therapy. Some of the results were disappointing. In contrast 52.6% claimed that they had an even better quality of life. ARBS showed slight better effect on quality of life than ACEI (lisinopril), compared to their effect on EF% ACEI (lisinopril) and ARBs (losartan or candesartan) showed the same effect, which means EF doesn't translate restrictively into QOL.

Conclusion:

It seems quite clear from totality of data presented that ACEI (lisinopril) and ARBS substantially reduce mortality and morbidity in patients NYHA class II-IV congestive heart failure caused by Left ventricular systolic dysfunction of all causes.It was found that there was a significant improvement on the EF% in the ARBS group as well as the ACEI (lisinopril) group, at the same time there was no significant differences when comparing the effect of the 2 groups of drugs on the EF%. The quality of life improved in most patients treated with these drugs.

Recommendations:

ACEI (lisinopril) and ARBS (losartan or candesartan) should be considered in all patients with LVSD unless there is contraindication.

ARBs (losartan or candesartan) should not be considered superior to ACE (lisinopril) inhibitors, but it could be an alternative drug to ACEI (lisinopril), in our study it has been shown high similarity in their effect on EF% with the ACEI (lisinopril).

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