

ORIGINAL ARTICL

Effect of Eplerenon on Heart Failure in patients with Paroxysmal Atrial Fibrillation and Ejection Fraction more than 45%

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ABSTRACT

Keyword: Eplerenon, atrial fibrillation, LVEF.

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Background: Atrial fibrillation (AF) is the commonest form of sustained arrhythmia; it increases the risk of stroke, heart failure and mortality. So, preventing AF episodes is needed. The aim of the present study was to investigate the effect of eplerenon (25mg) on cardiac functions in patients with paroxysmal AF. **Methods:** This was a Prospective Comparative Study, conducted at Cardiology department at Aswan University Hospital, on 100 patients with non valvular and paroxysmal AF, confirmed by electrocardiography divided into 2 groups: (Group A): 50 patients received eplerenon (25 mg) + amiodarone. (Group B): 50 patients received amiodarone only (control group). **Results:** After 6 months of follow up, we noticed a significant increase in left ventricular ejection fraction in group of patients who received eplerenon plus amiodarone in comparison with the group that received amiodarone only. **Conclusion:** Eplerenon is an effective drug in improvement of cardiac function in patients with non-valvular and paroxysmal AF when added to antiarrhythmic treatment (Amiodarone) .

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained arrhythmia and affecting millions of individuals worldwide, it associated with an increased risk of stroke, heart failure and all-cause mortality. The pathophysiology of AF is complex and multifactorial, involving electrical and structural remodeling of the atria. In patients with structural heart disease, such as heart failure, hypertensive heart disease or post-myocardial infarction (MI), the incidence and recurrence of AF are particularly high. This increased prevalence is largely due to underlying myocardial changes, such as fibrosis and atrial dilatation (1).

Atrial fibrillation characterized by irregular and rapid rhythm, leading to inefficient blood flow and a range of cardiovascular complications, heart failure stands out as one of the most serious and prevalent ,contributing to the morbidity and mortality associated with AF (2)..

The pathophysiological mechanisms linking AF and heart failure may attributed to that , AF can precipitate heart failure by reducing cardiac output , promoting structural changes in the heart , and increasing the risk of thromboembolic events. Conversely, heart failure creates an environment conducive to the development of AF by promoting fibrosis and neurohormonal activation (3).

Mineralocorticoid receptor blockers (MRBs) are beneficial in systolic heart failure. Specifically, the MRB eplerenone (EPL) has been shown to reduce new-onset AF and recurrent AF in heart failure patients (4). Both angiotensin II and aldosterone elevations may lead to atrial and ventricular fibrosis and contribute to human AF. Experimental results suggest that aldosterone may cause a substrate for atrial and ventricular fibrosis and AF .So we aimed in this study to clarify the effect of eplerenon (25mg) on cardiac function in patients with non-valvular and paroxysmal AF (5) (6).

SUBJECTS AND METHODS

A Prospective Comparative Study was conducted at Cardiology department at Aswan University Hospital, on 100 patients with non valvular and paroxysmal AF confirmed by electrocardiography then divided into 2 groups: **(Group A):** 50 patients received eplerenon (25 mg) + amiodarone. **(Group B):** 50 patients received amiodarone only (**control group**). Patients with non valvular and paroxysmal AF underwent cardioversion to sinus rhythm were included in the study. Patient with valvular heart disease, thyroid abnormalities, renal dysfunction, electrolytes abnormalities, acute coronary syndrome, pregnancy ,myocardial dysfunction with LVEF less than 45 % or on current use of mineraloreceptor antagonists were excluded from the study.

All the study populations were subjected to the following:

- Informed consent was obtained from each participant.
- **Resting ECG (Baseline ECG):**
 - Twelve lead ECG to detect rhythm, heart rate.
- **Transthoracic echocardiography:**
 - Transthoracic echocardiography was performed for each patient to exclude significant valvular heart disease, evaluate left ventricular ejection fraction, diastolic function, LV dimension, valve morphology and function.
 - All echocardiographic data were obtained using a commercially available machine (**Vivid 7, GE Medical System, Horten**) . In the apical four chamber view, the Simpson method was used to assess LVEF.
- **Follow-up visits:**
 - Transthoracic echocardiography was done after 6 months to evaluate LVEF, LV dimensions.

Ethical Consideration:

The study was approved by the Institutional Ethics Committee Faculty of Medicine, Aswan University. Moreover, a written consent was given by the surrogate decision maker.

Statistical examination

Data were entered into the computer and analyzed using version 20.0 of the IBM SPSS software program. (Armonk, New York: IBM Corporation) Quantitative and percentage descriptions were provided for qualitative data. The Kolmogorov-Smirnov evaluation was used to determine the distribution's normality. The range (minimum & maximum), mean, standard deviation, median and interquartile range (IQR) were used to describe quantitative data. At the 5% significance level, the derived results were deemed significant.

The used Evaluations were:

- 1 - **Chi-square test** for categorical variables, to compare among different groups
- 2 - **Student t-test** for normally distributed quantitative variables, to compare between two studied groups

RESULTS

This study was conducted on 100 patients admitted to cardiology department at Aswan university hospital with non-valvular and paroxysmal atrial fibrillation and underwent cardioversion from September 2022 to end of 2022. The patients were divided into 2 groups. **Group A:** 50 patients received eplerenon (25 mg) + amiodarone after cardioversion. **Group B:** 50 patients received amiodarone only after cardioversion. There was no significant difference between both groups as regard LVEF, LVEDD, LVESD at base line ($P > 0.05$), after 6 months of follow up, we noticed a significant difference between both groups as regard LVEF ($p < 0.003$), left ventricular ejection fraction was significantly lower in group B compared to group A, (**table 1**). There was a significant difference between both groups as regard hospitalization due to heart failure. Hospitalization due to heart failure was significantly higher in group B compared to group A, (**table 2**)

Table 1: Comparison between the studied groups as regard Echocardiographic parameters

Baseline	Group A (n=50)	Group B (n=50)	P
Left ventricular ejection fraction (%)	45.02±3.92	47.62±3.88	0.649
Interventricular septal thickness (mm)	8.1± 1.5	9.1± 1.4	0.64
Left ventricular posterior wall thickness(mm)	8.2 ± 1.4	9.14± 1.35	0.83
Follow up			
Left ventricular ejection fraction (%)	49.78±8.92	44.12±6.51	<0.003*

Interventricular septal thickness (mm)	9.08± 1.5	9.2± 1.4	0.63
Left ventricular posterior wall thickness (mm)	8.2 ± 1.4	9.35± 1.50	0.82

Table 2: Comparison between the studied groups as regard Primary Outcome, Secondary Outcomes.

	Group A (n=50)	Group B (n=50)	P
Primary outcome			
Death from cardiovascular causes or hospitalization for heart failure	0	0	-
Secondary outcomes			
Death from cardiovascular causes	0	0	-
Hospitalization for any reason	6	6	-
Hospitalization for heart failure	4	11	0.011*

DISCUSSION

Atrial fibrillation (AF) is the most common sustained arrhythmia and affecting millions of individuals worldwide. It associated with an increased risk of stroke, heart failure and all-cause mortality. The pathophysiology of AF is complex and multifactorial, involving electrical and structural remodeling of the atria. Non-paroxysmal AF (including persistent and permanent AF) increases the risk of thromboembolism and death, which calls for development of new upstream therapies to prevent AF progression (7). So this study was conducted to investigate the potential benefit of eplerenone (25mg) on cardiac functions in patients with non-valvular and paroxysmal AF especially when added to antiarrhythmic treatment (Amiodarone).

This study was conducted on 100 patients with non valvular AF admitted to cardiology department at Aswan university hospital for cardioversion from September 2022 to November 2023.

Patients were divided into 2 groups: Group A: 50 patients received eplerenone (25 mg) + amiodarone. Group B: 50 patients received amiodarone only post cardioversion of atrial fibrillation. (Control group).

At baseline in our study there was no significant difference between studied groups as regard Left ventricular ejection fraction (P=0.64),. But after 6 months of follow up, we noticed significant difference between both groups as regard left ventricular ejection fraction (LVEF) (p<0.003),LVEF was significantly improved in group A compared to

group B. This was in agreement with Lijnen study (8), that showed an increase of collagen and fibrosis in myocardial tissue in subjects treated with MRA. Mechanisms at the basis of this action are various. Lijnen proposed an involvement of angiotensin II acting through upregulation of angiotensin receptor subtype 1 induced by aldosterone.

There was a significant difference between both groups as regard hospitalization for heart failure, hospitalization for heart failure was significantly higher in group B compared to group A, this is in agreement with study that showed hospitalization for heart failure was significantly decreased with eplerenon.

CONCLUSIONS

Eplerenon is an effective drug in improvement of cardiac function in patients with non-valvular and paroxysmal AF when added to antiarrhythmic treatment (Amiodarone)

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