Effect of Aldosterone Antagonst, Spironolactone on Left Ventricle Remodeling After Acute Myocardial Infarction

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Abstract

This study was done in AL-KUT general hospital ,102 patients with ST-elevation acute myocardial infarction [STEMI],61 PATIENTS with anterior STEMI,41 patients with inferior[group 2].

Group 1 divided to two arms, the first arm received 25mg spironolactone daily, the second arm received the conventional therapy alone.

Group 2 was also divided to two arms, one receved 25mg spironolactone daily with conventional therapy,the other receved conventional therapy alone.

ECHO study was done one week, 1month and three months later.

In anterior STEMI left ventricular dilatation and dysfunction were less in arm one than in arm 2,while no differences in both arms in group 2.

الخلاصه

أجريت هذه الدراسه في مستشفى الزهراء العام في الكوت وقد تم جمع 102 حاله احتشاء العضله القلبيه الحاد الكامل . 61 حاله مصابين با الاحتشاء الامامي الكامل و41 حاله مصابه بالاحتشاء الخلفي الكامل وقد قسمت المجموعه الاولى الى ذراعين ، الذراع الاول استلم علاج spironolactone 25mg با الاضافه الى العلاج الروتيني ،والذراع الثاني استلم العلاج الروتيني فقط.

المجموعه الثانيه قسمت الى ذراعين ايضا ،ذراع استلم علاج spironolactone 25 mg با الاضافه الى العلاج الروتيني والذراع الثاني استلم العلاج الروتيني فقط .

وقد تم اجراء فحص الايكو بعد اسبوع، شهر واحد، وثلاثه اشهر لكافه المرضى.

وفي مجموعه الاحتشاء الامامي ، الذراع الاول كانت نسبه توسع البطين الايسر وبالتالي عدم كفاءه البطين اقل من الذراع الثاني في حين لايوجد فرق مهم بين الذراعين في حاله الاحتشاء الخلفي .

Introduction

Acute myocardial infarction (AMI)is the most common life-threatening disease occurring in technically advanced country.[1]. AML result from prolonged myocardial ischemia, precipitated in most cases by an occlusive coronary thrombus at the site of a preexisting atherosclerotic plaque. More rarely, infarction may result from prolonged vasospasm, inadequate myocardial blood flow, or excessive metabolic demand. Very rarely, AMI may be caused by embolic occlusion ,vasculitis, aortic root or coronary dissection, or aortitis, cocaine is a cause of AMI especially in young patients without risk factors.[2], after AMI the left ventricle (LV)undergo series of changes in shape, size and thickness in both infracted and non infracted segments, this process is referred to as ventricular remodeling and generally

precedes the development of LV dilatation and clinically evident heart failure in months or years after infarction.[3]

Angiotensin-converting enzyme inhibitors(ACE-I)have been studied extensively in patients with ST-segment elevation AMI, this agents appear to prevent the infarct remodeling to occur after large antero-apical AMI, data support the initiation of ACEI within the first 24hs after AMI.[4]

Nitrate (intravenous or oral) has favorable effect on ischemic process and prevention of dilative remodeling. [5]

Objective

To investigate the effect of spironolactone (Aldacton) which is aldosteron antagonist ,on (LV)remodeling ,LV dimensions and LV dysfunction after ST-elevation myocardial infarction(STEMI).

Method and Material

We collect 108 patients with ST-elevation AMI(STEMI) whose admitted to coronary care unit (CCU)of AL-KUT-general hospital, during the last four years, we missed six patients due to different causes ,the remaining 102 patients , 61patients with anterior STEMI (25 female and 36 male) and 41 patients with inferior STEMI (15 female and 26 male).

We exclude from the study the critically ill patients, patients with persistent hypotension from any cause e.g. right ventricular infarction, patients with previous history of heart failure or LV dilatation.

Anterior STEMI group divided to two arms, one arm (31 patients) received 25mg spironolactone (once daily) in addition to the conventional therapy, and the second arm (30 patients) received routine therapy alone.

Inferior STEMI group also divided to two arms, one arm (21 patients) received 25mg spironolactone (once daily) plus the conventional therapy, and the other arm (20 patients) received the conventional treatment alone.

The conventional therapy include thrombolytic agent (alteplase) and nitrates (initially), ACE-I or angiotensin-receptor blockers (ARB), B-blocker (if not contraindicated) and statines.

In both groups (anterior and inferior AMI) the spironolactone was started within 3 day after AMI.

ECHO study was done 3days,one month and three months after AMI to detect left ventricle end diastolic dimension(LVEDD), left ventricular end systolic dimension(LVESD)and LV dysfunction.

Result

Patients with anterior AMI who received spironolactone plus conventional therapy [arm one] have less left end diastolic dimension, left ventricular end systolic dimension and better LV function, in comparison with patients who had anterior AMI who received conventional therapy alone (arm two). Six patients in (arm one) had LVEDD more than 6mm versus sixteen patients in (arm two) after three months of the treatment. (P-value =0.01), table 1.

In the inferior AMI there were no differences between patients who received spironolacton plus conventional therapy [arm one] and patients who received conventional therapy alone (arm two). Four patients in (arm one) developed LVEDD more than 6mm. versus five patients in (arm two) which is of no clinical or statistical significance (P value = 0.6), table 2.

Table 1

Anterior MI	Spiranolactone	Conventional therapy	Total	P value
Improved	25	14	39	0.01
Not	6	16	22	
Total	31	30	61	

Table 2

Inferior MI	Spiranolactone	Conventional therapy	Total	P value
Improved	17	15	32	0.6 (NS)
Not	4	5	9	
Total	21	20	41	

Discussion

After the initial insult precipitate heart failure (particularly after AMI), progressive alteration occur in myocardial structure and function owing to continuing damage by underlying process and response to homodynamic stress and neurohumoral activation.

The left ventricle progressively dilate and change from normal ellipsoid shape to more spherical shape, this remodeling is accompanied by changes in the cardiac interstitium, leading to altered orientation of myofibrils and progressive fibrosis.[6]

Myocardial injury can depress cardiac function, which in turn causes activation of the renine-angiotensine-aldostrone system (RAAS) and the elaboration of endothelin and cytokines such as tumor necrosis factor (TNF).RAAS activation lead to increase concentration of angiotensin II and aldosteron, the former contributing to excess vasoconstriction and stimulate cardiac hypertrophy, the later lead to retention of salt and water, and cardiac fibrosis. [7]

Aldosteron blockade (AB) has found increasing use in patients with severe heart failure due to systolic left ventricle dysfunction based on the result of the Randomized ALdactone Evaluation Study (RALES).[8]

Eplerenone Post acute myocardial infarction Heart failure Efficacy and Survival Study (EPHESUS) [9]-study of over 6600 patients with acute myocardial infarction complicated by evidence of systolic left ventricular dysfunction [ejection fraction <40%] and sign of heart failure showed that the selective(AB) eplerenone when administered at a dose of up to 50mg daily between days 3-14 after AMI, in addition to standard therapy which include reperfusion, aspirin, statines, ACE-I and B-blocker, resulted in 17% reduction in

cardiovascular mortality mainly due to 21% reduction in sudden cardiac death. The finding by Hayashi et al [10] ,which suggest early effect of aldosteron antagonist (spironolactone) on ventricular remodeling and collagen formation, as well as experimental and clinical studies showing an effect of [AB] on ventricular remodeling and collagen formation [11],without interference in myocardial scar healing, may explain the effectiveness of (AB) in EPHESUS on sudden cardiac death, in that myocardial stretch is associated with activation of various neurohormones, including angiotensinII and endothelin. A reduction in ventricular remodeling and collagen formation would also improve the homogeneity of ventricular conduction and hence reduce the likelihood for ventricular arrhythmias. [12]

More recently, experimental studies of myocardial damage and heart failure have suggested that release of cytokines such as tumor necrosis factor may result in an increase in reactive oxygen species (ROS) and prostaglandin E2, which can cross the blood brain barrier and activate mineralocorticostroid receptors, which result in an increase in central sympathetic drive [13]. Aldosterone-blocking agents may therefore play an important role in improving myocardial norepinephrine uptake and decreasing central sympathetic drive [14].

Conclusion

In patients with anterior STEMI, spironolactone combined with routine treatment could inhibit left ventricle dilatation and left ventricle remodeling, and consequently left ventricular failure.

In patients with inferior STEMI, no significant differences in prevention of remodeling or dilatation of left ventricle were found between patients received spironolactone plus the routine treatment and patients who received routine treatment alone.

Effectiveness of Aldosterone-blocking agents during the early phase of AMI suggest that these agents will be an important addition to the current therapy.

References

1. Alpert,Joseph S. chap.15 ischemic heart disease ,manual of cardiovascular disease ,diagnosis and therapy-Joseph S.Alpert,Gordon A. Ewy,5th edition ,2002 , 204.

2. Myocardial infarction redefined-consensus document of The joint European society of cardiology – American college of cardiology committee for the redefinition of myocardial infarction. Am coll cardiol 2000;36;959.

3.Elliot M.Antamn, E.Braunwald, acute myocardial infarction, chap. 243,Harisson,s principles of internal medicine 15th.edition,2001 McGraw-Hill, p.1394

4Steven R.Omeen,Rick Nishimura part 4-Cardiology, Thomas M. Habermann, Mayo clinic international medicine 2004-2005. p.105

5 Jeffrey L. Anderson. ST elevated AMI and complication of myocardial infarction.chap.69 Goldman, Ausiello, Cecil, Textbook of medicine V.1 22nd edition, Saunders ,2004, P.419

6.Massie B.M. chap.55,heart failure pathophysiology and diagnosis, Cecil, Textbook of medicine V.1 22nd edition, Saunders ,2004 ,P.295.

7.Braunwald E,chap.215,Normal and abnormal myocardial function, Harrison, principles of internal medicine;16th edition;McGraw-Hill;2005;P1366.

8.Pitt B,Zannad F,Remme WJ,et al.The effect of spironolactone on morbidity and mortality in patients with severe

heart failure Eng J Med.1999,341,709-717.
9.Pitt B,Remm WJ,Zannad F,et al, Eng. J Med.,2003,348,1309.
10.Hayashi M, Tsutamoto T,Wada A, et al, Circulation,2003,107,2559.
11.Suzuki G,Morita H,Mishima T,et al. Ciculation,2002,106,2967.
12-Guideri G, Death Life sci.1983,33,1353 [CrossRef] [Medline].
13.Zhang Z.H,Francis J,Weiss RM,et al Am J Physio Heart Circ physiol,2002,283,1423.
14.Pitt B, Circulation,2003,107,2525.