

Role of spironolactone in heart failure

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Spironolactone is a potassium sparing diuretic that was originally developed in the early 1970s, as a competitive antagonist of aldosterone for the treatment of hyperaldosteronism, hypokalemia and edematous status as nephrotic syndrome. Recent studies on this drug has concentrated on its effect in patients with left sided H F as an aldosterone antagonist . It is postulated to work synergistically with ACEIs to provide more thorough blocking of the of the renin-angiotensin system

The effects of Spironolactone in patients with heart failure include:

1-On Renin-angiotensin -aldosterone system (RAAS):

RAAS is the complex mechanism by which the kidneys- control the cardiovascular system. In patients with heart failure the decreased renal flow is not due to low blood volume but to a heart pump that is not working efficiently.

ACEIs block the conversion of vasoconstrictor angiotensin I to the much more potent angiotensin II; also suppress the production of the Na⁺-retaining hormone aldosterone. Recent evidence indicated that aldosterone levels increased in patients with heart failure despite the suppression of angiotensin II.

Some abnormal conditions such as increased serum K⁺ and decreased hepatic clearance of aldosterone act as activators for aldosterone release in heart failure. Spironolactone is a specific aldosterone antagonist; it is competitively binding to the aldosterone receptor site in the distal convoluted tubules of the kidney preventing the formation of a protein important in the Na⁺-K⁺ exchange in the kidneys. This action causes increased amount of water and Na⁺ to be excreted while K⁺ is conserved, by this way Spironolactone prevent water- Na⁺ retention.

2- on autonomic nervous system:

It is found that Spironolactone reduces Norepinephrine uptake by the myocardium, improves baroreflex function and enhances Para sympathetic activity.

3- on remodeling changes of the heart:

Spironolactone reduces collagen build up which is a critical component of cardiac remodeling and improves heart size when combined with ACEIs.

4- on myocardial contractility:

Its active metabolite canrenone has been found to improve myocardial contraction, an additional action which may prove its beneficial effect in heart failure.

5- on trans cardiac aldosterone extraction:

Spironolactone inhibits the trans cardiac aldosterone extraction which is increased in patients with heart failure.

6- on pro-inflammatory cytokines:

Spironolactone inhibits the production of pro inflammatory cytokines (interleukin 16, tumor necrosis factor alpha and interferon gamma), these cytokines take part in the promotion and progress of heart failure .

7- It improves endothelial function and has an antiarrhythmic action and improves heart rate variability .

8- It corrects hypokalemia and hypomagnesemia that induced by loop diuretics .

9- Experimentally it is approved that Spironolactone prevent myocardial fibrosis .

10- Spironolactone increases nitric oxide bioactivity and suppress vascular conversion of ATI to AT II.

11- It reduces the hospitalization rate by 35% and the mortality rate by 30% in patients with heart failure .