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The effect of eplerenone on fibrosis in hypertrophic cardiomyopathy. A randomised controlled trial assessed using cardiopulmonary exercise testing and cardiovascular magnetic resonance

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Topic(s):
Chronic Heart Failure: Pharmacotherapy

Citation:

Background:
Recent studies have implicated aldosterone, a hormone of the renin-angiotensin-aldosterone system to cardiac hypertrophy, and cardiac and vascular fibrosis in cardiomyopathy. High levels of circulating aldosterone have been shown to cause myocardial and aortic fibrosis in animal models. In humans, high aldosterone concentrations have been associated with endothelial dysfunction, myocardial infarction, left ventricular hypertrophy and death. Aldosterone antagonism with spironolactone or eplerenone reverses the process of fibrosis in animal models.

Purpose:
Left ventricular dysfunction due to hypertrophic cardiomyopathy (HCM) is a disorder associated with an increased risk of morbidity and premature mortality. An important pathological feature seen in cardiomyopathy is the development of fibrosis and its association with functional impairment and arrhythmia, including predisposition to sudden cardiac death. This trial observes the effect of eplerenone on myocardial fibrosis and exercise tolerance in patients with HCM.

Methods:
42 patients were recruited into a double-blinded, placebo-controlled randomised study. Each patient had an established diagnosis of HCM without exclusion criteria (figure 1). 2 patients withdrew before enrolment. Enrolled patients were established on maximally tolerated doses of standard drugs used in the treatment of HCM and the doses of these drugs remained unchanged in the 2 months preceding enrolment to the trial. Patients were randomised to receive a maximal dose of 50mg eplerenone (n=21) or placebo (n=19). The patients underwent cardiopulmonary exercise testing and cardiovascular magnetic resonance (CMR) scan at baseline and 52 week follow up.

Results:
At 52 weeks follow up there was no difference between placebo and treatment groups in peak oxygen consumption (-1.05 vs 0.63, p=0.32), anaerobic threshold (0.4 vs 1.45, p=0.31) or ventilatory efficiency slope (-0.77 vs 1.76, p=0.065). In addition, there was no significant difference observed in LV mass or fibrosis as assessed by CMR.

Conclusion:
In the first randomised controlled trial using eplerenone in humans with HCM, we report no effect of treatment after 52 weeks on exercise capacity compared with placebo. In addition, we report no effect of treatment on the presence of fibrosis detected by CMR. Interpretation of these results are limited by small sample size and further studies will require a multi-centre recruitment process. The data presented here support the feasibility of eplerenone treatment in patients with HCM and provide statistical power calculation for future trials.
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INCLUSION CRITERIA
Stable patients with an established diagnosis of cardiomyopathy as assessed by history, examination and typical ECG/Echo findings who are on maximally tolerated doses of appropriate drugs with no changes being made to the prescription in the 2 months preceding the start of the trial.

EXCLUSION CRITERIA
- Patients already established on treatment with an aldosterone antagonist
- Patients with contraindications to eplerenone (hyperkalaemia, renal failure)
- Critically ill patients requiring respiratory and/or circulatory support
- Pacemaker or ICD at time of recruitment.
- Implanted ferromagnetic cerebrovascular clips
- Pregnant women (precautionary only)
- Intolerance of confined spaces
- Inability to lie supine for 60 minutes
- Unwilling or unable to give written informed consent
- Atrial fibrillation or ventricular bigemini.
- Any contraindication to CMR.
- Recent MI
- HCM patients who have received surgical/alcohol ablation treatment
- Use of NSAIDS
- Aged under 18 years
- Concomitant conditions associated with collagen turnover