Diltiazem Treatment for Pre-Clinical Hypertrophic Cardiomyopathy Sarcomere Mutation Carriers A Pilot Randomized Trial to Modify Disease Expression.

Definitions:

Sarcomere – The basic structural unit that makes up muscle.
Hypertrophy - Thickening
Double Blind – Neither the participants nor the researchers know who is given the drug vs. the placebo
Controls – Group given the placebo in a study
LV thickness-to-dimension ratio – This measurement looks at the thickness of the left ventricular wall in comparison to the dimension of the cavity.

Objective To determine the effectiveness of the drug Diltiazem in changing the expression of Hypertrophic Cardiomyopathy (HCM) in someone who carries the gene for HCM but has not yet been diagnosed with the condition. If successful this means that the progression and emergence of the disease could be modified prior to the onset of the disease.

Background HCM is caused by genetic mutations in the sarcomere - most commonly mutations in MYH7 and MYBPC3 genes. It is characterized by left ventricle hypertrophy (LVH) and small LV cavity size and causes an increased risk of heart failure and sudden death. HCM typically cannot be diagnosed early in life, although subtle characteristics can be observed in someone who carries the mutation.

Methods In a double blind trial, 38 subjects who had the HCM sarcomere mutation but have normal LVH were given either Diltiazem or the placebo. The age of the participants was on average 15.8 years. Treatment duration ranged from 12 to 42 months. Study procedures included electrocardiography (EKG), echocardiography (echo), cardiac magnetic resonance imaging (MRI) and blood tests.

Results Diltiazem was not associated with any serious negative reactions. Heart rate and blood pressure did not differ significantly between groups. However, LV cavity size progressively improved in the diltiazem-treated participants but did not in controls. Improvements were also seen in the ratio of the thickness and internal size of the left ventricle in those treated with diltiazem versus the placebo. A greater potential benefit was seen in those participants who carried MYBPC3 mutations and received diltiazem.

Conclusions Administration of Diltiazem is safe for adults and children, and may help modify the progression and emergence of the disease in people who carry

sarcomere mutations that cause HCM. More work is needed to better understand how to develop and implement new strategies to change disease progression.

Gaining more knowledge of how HCM develops and how we can slow or prevent disease progression will allow a transformation in the care of patients and families. Such advances would allow the cardiologist to take a proactive approach, rather than the passive, watch and wait approach currently used