Effectiveness of Fludrocortisone and Salt in Preventing Syncope Recurrence in Children. A Double-Blind, Placebo-Controlled, Randomized Trial

Salim MA, Di Sessa TG. J Am Coll Cardiol 2005;45:484–8.

Study Question: Is the combination therapy of fludrocortisone and salt more effective than placebo in preventing recurrences of syncope in pediatric patients with neurocardiogenic syncope confirmed by positive tilt table testing?
Methods: A prospective, double-blind, placebo-controlled clinical trial was performed in a cohort of patients with tilt test–confirmed neurocardiogenic syncope, all of whom were under 18 years of age. Subjects were randomized into two groups for 1 year of treatment. The two groups were (i) fludrocortisone and sodium chloride daily and (ii) two placebo capsules daily. All patients received education and counseling about syncope mechanisms and exacerbating factors. Follow-up during and after the study period was by regular clinical visits or written or phone-administered questionnaire. The primary outcome variable of the study was recurrence of syncope.
Results: Thirty-three patients were enrolled in the study, with follow-up data available on 32 patients at the conclusion of the trial. There were 18 children in the treatment group and 14 patients in the placebo group. The patient groups were similar for clinical factors such as the age at first symptoms, number of episodes, height/weight, duration of therapy, and other measures. Recurrent syncope occurred in 10 of 18 of the patients on pharmacologic therapy while they were receiving the medications. Recurrent syncope occurred in 5 of 14 patients in the placebo group, but all the recurrent symptoms occurred after ceasing therapy.
Conclusions: There is a significant placebo effect in the treatment of neurocardiogenic syncope with patients receiving placebo, experiencing fewer recurrences of syncope compared to those patients on standard therapy with fludrocortisone and salt.
Perspective: Randomized, double-blind, controlled trials are generally regarded as the gold standard in clinical research, particularly in assessing the value of a particular pharmacologic therapy. Data from such trials are often lacking when pediatric cardiologists are considering therapeutic options for their patients as many drugs have not been specifically tested in children. Having pediatric clinical trial data is always welcome, though in this case it must make pediatric cardiologists pause as they consider how to best treat patients with neurocardiogenic syncope. Treatment of syncope is a challenge. Patients and families usually are quite interested in treatment to avoid these troublesome events, yet several studies show a syncope recurrence rate of ~50% with a variety of treatment options including medications. Though this is a relatively small study, it found that an inactive agent (placebo) was actually more effective than an active agent in preventing recurrent syncope. This would suggest that we may need to significantly rethink our therapeutic approach to this usually benign, but clinically bothersome, syndrome. SW

Distinct Heritable Patterns of Angiographic Coronary Artery Disease in Families With Myocardial Infarction

Fischer M, Broeckel U, Holmer S, et al. Circulation 2005;111:855–62.

Study Question: Is there a genetic basis for specific morphologic characteristics of coronary artery disease (CAD)?
Methods: The investigators retrospectively reviewed the coronary angiograms of 882 patients all of whom had at least one sibling also affected with CAD. The angiograms were reviewed in detail and scored for a number of phenotypic characteristics of CAD, including degree of stenoses, site of stenoses, morphology of stenoses (length, presence of ectasia) and presence of calcifications. Information about other cardiovascular risk factors and other clinical information was obtained by standardized questionnaire and confirmed by retrospective medical record review. Statistical analysis of the data was performed to determine heritability estimates for various phenotypic features.
Results: The researchers found a significant heritable risk for proximal coronary stenoses, particularly stenoses in the left main coronary, as well as increased heritable risk for the presence of coronary artery ectasia and coronary calcification. Distal disease, number of diseased vessels, and length of the lesions did not appear to have a significant heritable component.
Conclusions: Some morphologic characteristics of CAD, such as proximal disease as well as presence of ectasia and/or calcification, appear to have a significant genetic influence on their occurrence.
Perspective: It is well known that a positive family history is one of the most important risk factors for CAD in an individual patient. Despite this, recent genome-wide searches for specific regions of the genome that can be reproducibly linked to the CAD phenotype have been largely unsuccessful. Possible reasons for this lack of success include the fact that CAD is likely a multifactorial disease with many genes contributing to its occurrence as well as the fact that the contribution of each individual gene change to the observed phenotype may be quite small. These investigators point out another aspect of the problem: CAD is phenotypically diverse, and more specific characterization of a subject's disease prior to genome-wide searches may be helpful in ultimately detecting reproducible linkages to specific areas of the genome, and particular gene changes. Optimal and detailed phenotypic characterization of subjects and their clinical findings in sufficiently