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Elimination of cardiac arrhythmias using oral taurine with L-arginine with case histories: Hypothesis for nitric oxide stabilization of the sinus node

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Summary We searched for nutrient deficiencies that could cause cardiac arrhythmias [premature atrial contractions (PACs), premature ventricular contractions (PVCs), atrial fibrillation, and related sinus pauses], and found literature support for deficiencies of taurine and L-arginine. Case histories of people with very frequent arrhythmias are presented showing 10–20 g taurine per day reduced PACs by 50% and prevented all PVCs but did not prevent pauses. Adding 4–6 g of L-arginine immediately terminated essentially remaining pauses and PACs, maintaining normal cardiac rhythm with continued treatment. Effects of taurine useful in preventing arrhythmias include regulating potassium, calcium and sodium levels in the blood and tissues, regulating excitability of the myocardium, and protecting against free radicals damage. Taurine restored energy and endurance in one of the cases from a debilitated status to normal. Arrhythmias may also respond to taurine because it dampens activity of the sympathetic nervous system and dampens epinephrine release. L-arginine may have anti-arrhythmic properties resulting from its role as a nitric oxide (NO) precursor and from its ability to restore sinus rhythm spontaneously. Endogenous production of taurine and L-arginine may decline in aging perturbing cardiac rhythm, and these ''conditional'' essential nutrients therefore become ''essential'' and require supplementation to prevent morbidity and mortality. L-arginine is hypothesized to prevent cardiac arrhythmias by NO stabilization of the sinus node. Cardiac arrhythmias having no known cause in otherwise healthy people are hypothesized to be symptoms of deficiencies of taurine and arginine.

Introduction

Premature atrial contractions (PACs) and premature ventricular contractions (PVCs) [ectopic heartbeats] are common disorders of cardiac rhythm particularly in healthy older people. These arrhythmias are beats that occur early in either the atria or the ventricle, causing the heart to beat out of synchronization before the next regular heartbeat. In both cases, the heart seems to pause or hesitate until the next beat. Neither are usually considered to

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be serious cardiac events, and patients may have experienced them for many years with little cardiac distress, although they can be discomforting and annoying. Sinus pauses occur when the sinus node fails to generate an impulse for a few seconds, and long pauses require pacemakers.

Normally, the pacemaking activity of the sinus node suppresses impulse-production by other cardiac cells, but if conductance to some other part of the heart muscle is blocked, or if the heart is over stimulated, islands of cells may express their latent impulse-production ability, resulting in extra or early beats.

Common causes of these ectopic heartbeats among healthy persons are ingestion of caffeine, nicotine, alcohol, stress, hyperthyroidism, electrolyte imbalances, candida albicans infection and some medications. Avoidance of, or correction of, these initiators, and use of drugs such as beta-blockers and calcium channel blockers have long been used to treat patients with these ectopic beats with some success.

The literature was searched for natural anti-arrhythmic agents, ones that were potentially insufficient in the diet or insufficiently produced in the body, that might account for the occurrences of these cardiac arrhythmia when common causes had been ruled out. Nutrient deficiencies capable of producing arrhythmias included acetyl-L-carnitine, calcium, CoQ10, magnesium, potassium, selenium, taurine, thiamine, vitamin D3, vitamin E and zinc. For the individuals discussed below, none of these nutrients in supplemental form, except taurine, had beneficial effects in reducing their arrhythmias. The strong anti-arrhythmia effect of taurine was first noted when one person switched from magnesium glycinate to magnesium taurate, while using magnesium in an attempt to prevent arrhythmias.

In 1969, Novelli et al. [1] first reported taurine as having anti-arrhythmic effects. Since then there have been several dozen similar reports of benefit to cardiac rhythm. Effects of taurine useful in managing arrhythmias include regulating potassium, calcium and sodium levels in the blood and tissues [2], and regulation of the excitability of the myocardium possibly by modifying membrane permeability to potassium [3]. Arrhythmias may also respond to taurine because it dampens activity of the sympathetic nervous system and dampens epinephrine release, relaxing the individual [4]. In 2004, Hanna et al. [5] demonstrated the protective effect of taurine against free radicals damage in the myocardium.

Regardless of these benefits, the effects that were observed in treating PACs, PVCs, pauses and occasional tachycardia showed taurine to be helpful but inadequate to prevent all PACs and to completely restore normal sinus rhythm. Therefore, the search for nutrients that had anti-arrhythmic activity was continued.

While experimenting with humming to induce nasal nitric oxide (NO) production in the treatment of chronic rhinosinusitis, it was observed that PACs could be prevented simply by strong humming for an hour on each of four consecutive days and thereafter as needed [6]. The observation suggested that L-arginine, known to be a natural precursor of NO, might also have anti-arrhythmic properties. No previous reports showing benefit of L-arginine in preventing or treating arrhythmias was found, but we did find support for the notion that NO is a modifier of human sinus node automaticity [7]. Therefore, we hypothesized that L-arginine would be effective in preventing cardiac arrhythmias by induction of NO, thus stabilizing the sinus node.

L-arginine may be a natural anti-arrhythmic agent upon consideration of its effect in restarting normal sinus rhythm at the completion of heart surgery. For example, Kiziltepe et al. [8] used L-arginine for protection of acutely ischemic myocardium during surgery (coronary artery bypass grafting) in a study of 40 patients. They showed that L-arginine treatment increased NO levels and attenuated free O2 radical mediated myocardial injury relative to placebo. Controlled reperfusion with L-arginine enriched non-cardioplegic blood greatly diminished ischemia/reperfusion injury. Ninety percent of their L-arginine treated group had spontaneous return of the sinus rhythm after surgery, while 80% of the control patients required defibrillation ($P < 0.0001$). In addition to significantly better hemodynamics, perioperative myocardial infarction incidence was significantly lower, and the length of intensive care unit and hospital stays were each significantly shorter in their L-arginine study group than in the placebo-treated group without any deaths in the L-arginine treated group, but with one death in the control group.

After explaining to the subjects some of the promising benefits of NO, taurine and L-arginine in cardiovascular research, the anecdotal humming for arrhythmia observations, the efficacy and safety of taurine, and the potential for drug interactions with L-arginine, the following treatments were conducted in otherwise healthy people.

Materials and methods

A 64-year old male had suffered from very frequent (25,000 per day) PACs for 6 years, occurring with nearly every fifth beat. The PACs were accompa-

nied by physical weakness (greatly reduced energy and endurance not attributable to PACs or other cardiovascular disease) and occasional paroxysmal tachycardia, rendering him debilitated. Propranolol was not successful. Taurine (5 g with each meal and at bedtime) was taken daily. L-arginine (1.5 g) in gelatin capsules was taken with each meal and at bedtime. No drugs or pacemakers were used during amino acid therapy.

An 82-year old male had suffered from documented (24-h Holter) very frequent (21,000 per day) PVCs for 5 years. He also had 650 bigeminal events, 90 couplets and sinus pauses every sixth to tenth beat of about 2 s each with the longest being 2.2 s. His PVCs were responsive to verapamil, a calcium channel blocker, but it had no effect on the incidences of pauses. Verapamil was tapered off and taurine was substituted. He took 10 g (2.5 g with each meal and at bedtime) of taurine and 4 g (1 g with each meal and at bedtime) of L-arginine each day. No drugs or pacemakers were used during amino acid therapy.

A 60-year old man had cardiac arrhythmias (PAC/PVCs) for 6 years. The symptoms included strong palpitation, very rapid heart beats of over 150 beats per minutes, skipped beats, uneven heart rates, and some totally out of synchronization beats. Daily skipped beats happened most frequently. Out of sync heart beats awoke the man frequently at night. Holter monitor tests for 24 h, ultrasound, and stress test showed arrhythmias with occasional atrial fibrillation. He did not use drugs or a pacemaker to treat the arrhythmias. He began taking taurine with modest change in his symptoms resulting, and later added L-arginine. He used 4 g of taurine and 1 g of L-arginine three times a day with meals.

Results

The PACs in the 64-year old male were reduced by 50% with continued use of 20 g of taurine a day. Although the total number of ectopic beats per day was reduced, when they occurred at every fifth beat. Incidences of occasional paroxysmal tachycardia were reduced by half using taurine. Energy and endurance were restored to normal by taurine. Addition of L-arginine to the taurine protocol almost immediately stopped nearly all arrhythmias and prevented tachycardia for an observation period of more than 3 months. Remaining PACs numbered less than 100 ectopic beats per day. Missing doses of L-arginine usually precipitated arrhythmias.

The PVCs in the 82-year old male were completely prevented with continued use of 10 g of taurine per day, equal in effect to verapamil. However, the pauses remained. Addition of L-arginine immediately and completely terminated the pauses for the observation period of more than 3 months. Missing doses of L-arginine precipitated pauses, and missing doses of taurine precipitated PVCs.

The arrhythmias in the 60-year old male decreased dramatically (95—100% reduction) with elimination of heavy palpitations and atrial fibrillations upon addition of L-arginine to his taurine treatment. He remained symptom-free essentially all of the time. When he noticed arrhythmias, they were nearly always skipped beating and not fibrillations.

Discussion

These case histories are the first published evidence of taurine with L-arginine to treat and prevent common, normally benign, cardiac arrhythmias in otherwise healthy people. None of these subjects had accepted deficiency symptoms of either taurine or L-arginine. Each subject had tried many natural products, some drugs and life-style modifications with varying degrees of success. However, only the combination of taurine and L-arginine produced essentially complete prevention of arrhythmias and fibrillations for more than a 3-month period. Since each of these subjects had been using taurine for weeks to months prior to starting L-arginine, it is unknown what residual effects resulted from preconditioning with taurine.

Taurine is a conditionally-essential amino acid which is not utilized in protein synthesis, but is found free or in simple peptides. Taurine has been shown to be essential in certain aspects of mammalian development, and in vitro studies in various species have demonstrated that low levels of taurine are associated with various pathological lesions, including cardiomyopathy, retinal degeneration, and growth retardation. Metabolic actions of taurine include: bile acid conjugation, detoxification, membrane stabilization, osmoregulation, and modulation of cellular calcium levels. Taurine has been used in the treatment of: cardiovascular diseases, hypercholesterolemia, epilepsy and other seizure disorders, macular degeneration, Alzheimer's disease, hepatic disorders, alcoholism, and cystic fibrosis [9].

Some seafood (conch, inkfish, blood clams, shellfish, crabs, sole) eaten by long-lived Okinawans

and other oceanic fishing communities are rich sources of taurine (2500–8500 mg/kg), while meats and other foods eaten by Western societies are much lower in taurine.

As humans age, hepatic taurine synthesis can be reduced or fail completely, resulting in low to no energy, cardiac, digestive, and mental issues, and premature death. Since taurine has an important role in formation of bile salts and digestion, perhaps it is required in these larger amounts for the best absorption and utilization of L-arginine in the aged population, helping to explain these results with low doses of L-arginine.

Under normal conditions, the 3.5–5 g per day of arginine found in the typical Western diet would be marginally sufficient to maintain general health. Foods richest in arginine are often fatty and include: peanuts, peanut butter, cashew nuts, pecans, walnuts, almonds, chocolate, coconut, cereal grains, dairy products, gelatin, meat, oats, soybeans, and edible seeds. Foods highest in arginine are often avoided by the aged population sometimes on advice from physicians due to their fat content, and deficiencies become possible, perhaps precipitating arrhythmias.

Synthesis of arginine occurs principally via the intestinal–renal axis. Consequently, impairment of small bowel or renal function in aging or disease can reduce endogenous arginine synthesis, thereby increasing dietary requirements to prevent arrhythmias and maintain cardiovascular health.

L-arginine may have interactions with anticoagulants, antiplatelet and blood pressure drugs and it may change electrolytes in the blood. People taking coumadin may require less or none while taking L-arginine to prevent excessive blood thinning and bleeding. Arginine may significantly raise blood sugar levels in diabetes requiring changes to medication. Larger doses have been implicated in recurrence of latent herpes infections, a disease for which topical ionic zinc treatment is effective [10]. Many drug interactions are possible since arginine has many functions for which drugs are currently substituted. People with liver or kidney disease may be especially sensitive to these interactions and they should avoid using L-arginine except under medical supervision.

Large doses of arginine worsen inflammation in the lungs and can contribute to asthma and allergy symptoms. Taurine may impair the production of adrenaline, thus asthma symptoms may be increased. Magnesium throat lozenges (100 mg magnesium) are useful as preventative and as a rescue treatment for asthma, and also provide additional cardiovascular support. There may be similar benefits in preventing arrhythmias from taurine with resveratrol or other NO inducers, which might be useful in case of side effects from L-arginine.

Arginine is a precursor of nitric oxide, which causes blood vessel relaxation (vasodilation). Arginine is also useful in the treatment of medical conditions that are improved by vasodilation, including angina, atherosclerosis, coronary artery disease, erectile dysfunction, heart failure, intermittent claudication/peripheral vascular disease, and vascular headache. Arginine also stimulates protein synthesis and has been used in wound healing, bodybuilding, enhancement of sperm production, and prevention of wasting in people with critical illness.

People having had heart attacks who were receiving ''standard postinfarction therapies'' had an increased incidence of death when L-arginine was added to the protocol. Blood levels of L-arginine in both treatment and placebo groups remained normal, and they did not increase or differ from those receiving identical treatments without arginine. Added arginine did not improve vascular stiffness or left ventricular function [11]. We were unable to ascertain from this article drugs used with L-arginine to discuss any possible interactions.

Caffeine and the drugs digoxin and isoproterenol, suspected or proven arrhythmia inducers, can greatly reduce the arginine content of cytosol in both ventricular and atrial heart muscles of animals [12]. Experimental dosing of rats with toxic doses of caffeine (15 mg/kg/min) led to ectopic beats and lethal fibrillation, which responded somewhat by treatment with propranolol or verapamil [13]. We suggest that these observations support our hypothesis that L-arginine is vital in maintaining normal sinus rhythm.

Nitric oxide (NO) is derived from oxidation of L-arginine by NO synthases. NO is an agent with wide-spread functions including maintenance of vascular tone, neurotransmitter function in both the central and peripheral nervous systems, mediation of cellular defense, cellular respiration, generation of reactive oxygen species, inhibition of platelet aggregation and adhesion, and modulation of smooth muscle cell proliferation. NO has been implicated in a number of cardiovascular diseases. Virtually every risk factor for cardiovascular diseases appears to be associated with a reduction in endothelial generation of NO. Reduced basal NO synthesis or action leads to vasoconstriction, elevated blood pressure and thrombus formation. By contrast, overproduction of NO leads to vasodilatation, hypotension, vascular leakage, and disruption of cell metabolism [14]. There is also an inverse relationship between arginine intake and

C-reactive protein, further suggesting increased NO generation [15]. However, NO has not been reported previously to have anti-arrhythmic properties. Enhanced NO production occurs during magnesium deficiency which lowers red blood cell glutathione [16]. This may explain why one severely magnesium deficient man believed that magnesium supplements worsened his arrhythmias.

With the discovery that caloric restriction, a promising means of life extension, induces NO production [17], interest in nitric oxide and its precursors will likely increase. Consequently, interest in oral use L-arginine with the intent of producing cardioprotective benefits and life extension will likely remain high.

If the biosynthesis of taurine and L-arginine becomes inadequate in aging, they become essential nutrients rather than ''conditional'' essential nutrients. Unnecessary morbidity, such as cardiac arrhythmias, and mortality result if they are not supplemented in sufficient amounts [18]. Drugs should not be substituted for nutrients. It is hypothesized that doses of taurine in the 10–20 g per day range combined with L-arginine in doses of 3–6 g per day, will be found effective in the prevention of cardiac arrhythmias in clinical trials, and such trials are highly recommended. We hypothesize that cardiac arrhythmias not having a specific cause in otherwise healthy people are symptoms of nutrient deficiencies of taurine and L-arginine.

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