Testosterone as an atrial fibrillation treatment and stroke preventative in aging men: Case histories and hypothesis

Correspondence/Medical Hypotheses 75 (2010) 269-274

1o caso: 59-year old man.
The elderly subject had an initial serum TT level of 361 ng/dl. He received natural testosterone (20 mg in AM and 20 mg in PM) as a % aqueous, sublingual/buccal liquid, slowly swallowed over a 30-60 min period. He had AF daily for 1 year prior to TT treatment. He was also taking warfarin, a beta-blocker (metoprol ER) and a calcium channel blocker (diltiazem ER), but no rhythm drugs. His blood pressure, cholesterol and CRP were normal. Other than pre-atrial contractions (PACs) for the preceding 10 years, he had no other heart conditions according to an MRI and history. His serum TT rose to 463 ng/dl within 14 days of initiation of TT treatment, and to 1489 ng/dl within 45 days, with each measurement being taken mid-day. NSR and no instances of AF and only a few instances of PACs were observed in seven weekly EKGs and by direct observation after the second week of TT treatment. His INR changed from 2.5 to 5.4 upon treatment with TT, requiring substantial reduction in warfarin.

2o caso: The 59-year old subject with strongly symptomatic nocturnal paroxysmal AF and depression received both DHEA (25 mg/day) and natural testosterone (50 mg/day) as a gel applied to his shoulders. His serum mid-day TT levels at initiation of TT treatment was 150 ng/dl, much lower than normal. He was also being treated with warfarin, a rate drug (sotalol) and a rhythm drug (dofetilide). Previously, he had congestive heart failure and persistent AF which had been treated with ablation and cardioversion. An MRI showed no cardiac damage. His depression and ectopics ended, and his observed AF episodes over a 45-day period rapidly declined after initiation of daily TT, with only two observed instances of overt AF lasting 5 min and 1 h after the first 2 weeks. Both subjects felt that TT was a necessary, superior and safe natural rhythm treatment for AF. Since beta-blockers lower testosterone in men [11], replacing TT when they are used in AF treatment appears essential. Rhythm drugs for AF have side effects sufficiently severe to recommend their initial administration in a hospital, and the apparent safety of treating AF with TT should be welcome. An increase in TT from exercise, carbohydrates, fats
and other TT boosters is also hypothesized to be helpful in AF treatment. Illicitly obtained anabolic steroids as testosterone ethanate (250mg-1.5g weekly) and stanozolol (50-200 mg weekly), both via intramuscular injections over a 12-week duration caused rapid, highly symptomatic AF in a young male athlete/body builder [12], and similarly, 200 mg of testosterone cypionate, 200 mg of extrabolin decanoate, and 120mg of stanozolol 2 days per week for 5 weeks caused the same adverse symptoms in another young athlete/body builder [13].

Dear Dr. Charlton,
Testosterone (TT) may play an important role in treating atrial fibrillation (AF) and preventing stroke in aging men. AF increases [1], while TT declines in them [2]. In 2009, TT was first shown by Lai et al. [3] to be low in men with lone atrial fibrillation (lone AF) compared with non-AF controls (476 ng/dl versus 514ng/dl, p = 0.005). No significant differences were found in estradiol levels. They suggested that low TT is associated with susceptibility to lone AF in men. Similarly, serum dehydroepiandrosterone-sulfate (DHEA-S) was shown to be low in lone AF in men and in a number of other aging related illnesses as a non-specific indicator of aging and health status [4]. Deficiency of TT promoted arrhythmia in rat atria by mechanisms which induce calcium leakage from the sarcoendoplasmic reticulum helping to explain the increase in AF in association with low TT, particularly in elderly men [5]. Circulating TT levels in men have a diurnal variation, usually reaching a mean maximum level of 710ng/dl at approximately 6 AM and declining gradually to a mean minimum level of 426 ng/dl at approximately 10 PM, averaging about 610 ng/dl in mid-day and afternoon [6].

Stroke is a major disabling and sometimes lethal complication of AF, with ischemic strokes occurring 2-7 times more frequently in AF than in the general population [7]. Low testosterone is an independent risk factor for acute ischemic stroke, stroke severity and related death in men considering age, blood pressure, diabetes, ischemic heart disease, smoking and atrial fibrillation [8]. Low testosterone is also associated with coronary artery disease and with myocardial infarction in men [9], and all-cause mortality independent of numerous risk factors in men [10]. Beta-blockers, commonly used rate drugs in cardiology, lower testosterone in men [11], apparently increasing the risk of AF and stroke.
An elderly (69-year old) paroxysmal/lone AF subject often experienced normal sinus rhythm (NSR) early in the morning at the same time of day when TT is highest. Considering the literature and his experience, I hypothesized that low testosterone was the cause of his AF, and that increasing TT would terminate AF. I tested my hypothesis in this
Since both lower and higher than normal TT concentrations are associated with AF, blood levels of TT should not be elevated much in excess of the normal physiologic range in the treatment of AF.
These two cases are the first reports of TT treatment for AF and stroke prevention in men. These observations suggest the possibility of a safer and more effective natural rhythm treatment for AF and stroke prevention. Since TT blood levels of the two young athlete/body builders were not reported, I hypothesize that their levels were considerably higher than the 1489 ng/dl reported for my elderly AF-free subject. Large scale clinical trials to establish the extent of efficacy and safety are strongly recommended.

References

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doi:10.1016/j.mehy.2010.03.023