



Alternative Therapies in the Treatment of Atrial Fibrillation

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Abstract

Atrial fibrillation (AF) is the most common clinical arrhythmia and represents a major social and economic problem. The number of subjects with AF is constantly increasing as a result of aging and improved survival in several cardiac and non-cardiac diseases. Patients with AF are often symptomatic, have a reduced physical capacity and are at high risk for thromboembolic events. Moreover, AF is associated with increased mortality and independent of the management, based either on rhythm or rate control strategy. The safety and efficacy of most anti-arrhythmic drugs are questionable. Increasing attention has therefore been addressed to evaluate the possible therapeutic and/or preventive effects of forms of treatment coming from ancient medical traditions of Far East, like acupuncture and yoga. In traditional Chinese medicine, acupuncture has been found effective in managing patients with paroxysmal supraventricular tachycardia. Recently, also in the Western literature, reports have been published supporting the clinical efficacy of acupuncture to treat arterial hypertension and to reduce chest pain. Other studies have evaluated the effects of acupuncture and other methods of Eastern Medicine, i.e., Qigong, Tai Chi Chuan and Yoga, in the treatment of cardiac illnesses associated with supraventricular arrhythmias.

Two reports on the effects of acupuncture in preventing or reducing the rate of AF recurrences in patients with persistent or paroxysmal AF have been recently reported. Another ancient traditional eastern form of therapy and prevention, i.e., yoga, has been recently shown to reduce episodes of atrial fibrillation and improve the symptoms of anxiety and depression often associated with this arrhythmia. Growing evidence indicates that acupuncture and yoga are safe, without any pro-arrhythmic effect and with limited cost. All these factors should be considered when evaluating the efficacy of therapeutic intervention for an epidemic disease such as AF.

Introduction

Atrial fibrillation (AF) is the most common clinical arrhythmia and represents a major social and economical problem.^{1,2} The number of subjects with AF is constantly increasing as a result of aging and improved survival in cardiac and non-cardiac diseases. Patients with AF are often symptomatic, have a reduced physical capacity and are at high risk for thromboembolic events. AF is associated

with increased mortality and remains to be defined if a management based on rhythm control is better than a rate control strategy.^{2,3} To maintain sinus rhythm and to prevent recurrences, antiarrhythmic drugs are commonly used in spite of their limited efficacy and frequent adverse effects.⁴ Alternative strategies based on a direct targeting on arrhythmia mechanisms such as radiofrequency ablation or upstream therapies have provided contrasting results. The former

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approach may be properly used only in limited and selected groups of patients particularly when symptoms are invalidating.⁵ The antiarrhythmic efficacy of ACE inhibitors, statins, and fish oil has been disappointing when tested in randomized prospective studies.⁶⁻⁸

In the GISSIA AF, valsartan administration was unable to reduce the recurrence rate of AF in patients with paroxysmal or persistent AF.⁹ In the OPERA study, Omega-3 fatty acid supplementation did not prevent post-operative AF after cardiac surgery.¹⁰ Thus available evidence⁷⁻¹³ seems to be insufficient to drive changes in therapy management, and prompts the development of new therapeutical approaches.

Traditional Chinese Medicine

In traditional Chinese medicine, acupuncture has been found effective in managing patients with paroxysmal supraventricular tachycardia.¹⁴ Recently, also in the Western literature, reports have been published supporting the clinical efficacy of acupuncture to treat arterial hypertension¹⁵ and to reduce chest pain.^{16,17} Several other studies have evaluated the effects of acupuncture and other methods of Eastern Medicine, i.e., Qigong, Tai Chi Chuan and Yoga, on hemodynamic parameters or symptoms related to different cardiovascular diseases.¹⁸⁻²⁸

In the Traditional Chinese Medical Doctrine²⁹ AF, like most supraventricular arrhythmias, is related to Heart Yin deficiency in the absence of structural disorders or to Heart Yang deficiency in the presence of a cardiac disease. The Neiguan spot is located in the portion of the heart meridian situated in the forearm and is responsible for blood flow and pulse rate control. Its malfunction has been associated with anxiety and restlessness and cardiac pain.

In the Western world, puncturing of the Neiguan spot has been used to treat chest pain, sickness and vomiting during chemo-embolization procedures³⁰ and to limit the symptoms related to fullness-tension in the chest and palpitations.³¹ Reductions in the electrocardiographic signs of myocardial ischemia and plasma levels of endothelin have also been reported.^{31,32}

Electroacupuncture of the Neiguan spot has also been associated with an effect on the autonomic nervous system and, in particular on the sympatho-vagal interaction.^{33,34} In one of the first studies, Kong et al³⁵ was able to restore a more physiological sympatho-vagal balance after acupuncture by measuring heart rate variability. More recently, however, in a systematic review³⁶ in which the effects of acupuncture on heart rate variability were studied in different patient populations and experimental conditions, contrasting results were observed. For example in healthy subjects, acupuncture determined a significant attenuation of signs of sympathetic activation and reduced vagal modulation induced by a stress state in comparison to sham acupuncture.³⁷ Other studies, however, failed to detect similar changes in heart rate variability parameters when subjects were exposed to mental stress testing or other stressors.³⁶ On the other hand, Flachskampf et al,¹⁵ reported that 6 weeks of acupuncture significantly lowered median 24-h ambulatory blood pressure and that the effect was no longer present after cessation of acupuncture treatment.

The possibility that acupuncture may exert its anti arrhythmic effect through an action on the autonomic nervous system is therefore a plausible hypothesis although not tested in our studies. Indeed, several clinical and experimental reports have indicated that an imbalance of autonomic control mechanisms due to either an increase in vagal or sympathetic neural activity directed to the heart may favour the initiation and maintenance of AF episodes.^{1,2} In patients who developed AF during Holter recordings,^{38,39,40} signs of either an increased vagal or sympathetic modulation of the sinus node were commonly detected in the minutes preceding AF initiation: a finding that in our opinion, suggests that an imbalance between the two branches of the autonomic nervous system rather than a specific predominance of one component is the most important pro-arrhythmic factor.

The possibility that the antiarrhythmic effect of acupuncture might be related to a stabilization of sympathetic and vagal control mechanisms rather than to a direct antiadrenergic or vagomimetic effect is therefore appealing and is substantiated by recent experimental findings. In fact, whereas direct high threshold cardiac vagal ganglia stimulation has been associated with a pro-fibrillatory

effect^{40,41} bilateral low-level vago-sympathetic nerve stimulation has been found to suppress effectively high-frequency stimulation-induced focal AF at atrial and pulmonary vein sites.⁴²⁻⁴⁴ Whether acupuncture of Neiguan spot might exert similar effects on cardiac autonomic ganglia remains to be determined and at the moment it is an interesting hypothesis.

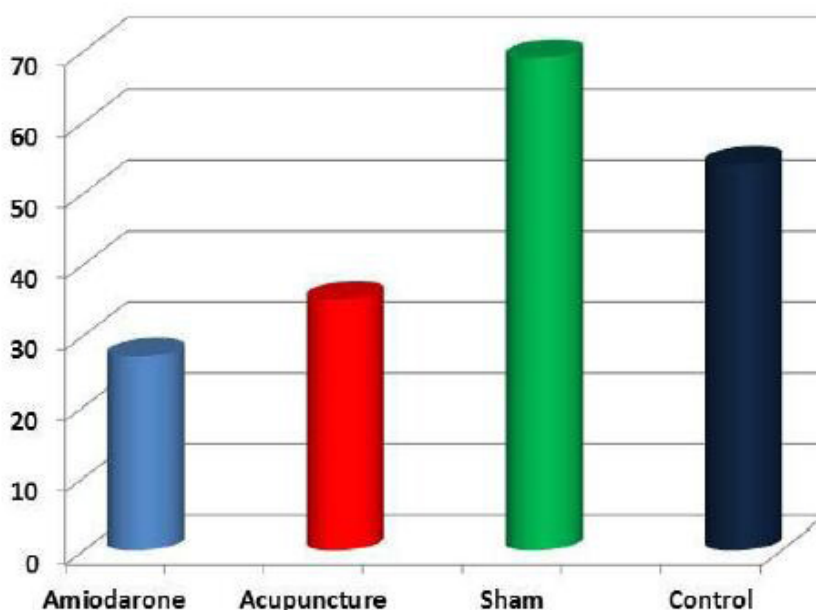
Our Experience

We have published two studies which evaluate the effects of acupuncture in preventing or reducing the rate of AF recurrences in patients with persistent AF and in those with paroxysmal AF. In the first study,⁴⁵ the antiarrhythmic efficacy of acupuncture (figure 1) was similar to that of amiodarone, the most effective antiarrhythmic drug used in the Western world to treat AF patients. Patients who responded to acupuncture were characterized by the traditional risk factors such as LVEF, hypertension, and LA diameter that are associated with AF recurrence^{1-4,46} thus confirming that our population was representative of that commonly encountered in clinical practice. Moreover, sham operated patients had an AF recurrence rate similar to patients with no antiarrhythmic therapy. Thus, specific site of acupuncture treatment rather than simple needling was the mechanism responsible for the observed antiarrhythmic effects. Unfortunately, we have

been unable to identify the mechanisms responsible of the effectiveness of acupunctural treatments. In addition to a modulatory action on autonomic control mechanisms, we cannot exclude that biochemical, psychological or placebo effects might have played a major role through endorphins or other chemical mediator releases reduced pain perception, improved sleep quality, anxiety sedation or acceptance of the presence of a disease.^{32,47} We have also observed that acupuncture showed its antiarrhythmic action preferably in the first months after electrical CV, the time frame that corresponds to the highest recurrence rate^{4,48} where autonomic mechanisms are likely to play a major role.^{38,39,49} Regarding this it is of interest to note that our patients were treated with acupuncture for a 10-week period, but the antiarrhythmic effect persisted throughout the whole study period.

The major limitations of our study was that it was conducted in a small number of patients and the amiodarone group consisted of patients who were not randomized but were on amiodarone treatment according to physician indication Nevertheless, there was adequate power to detect differences among the study groups. AF recurrences were determined by the presence of the arrhythmia during scheduled control visits or during exams requested by patients after the occurrence of symptoms. There was no trans-telephonic monitoring system to detect also asymptomatic or brief

Figure 1: Cumulative Percentage of AF Recurrence in the Different Groups



self-terminating AF episode. In spite of the above limitation, this was the first randomized study that showed that acupunctural treatment was safe and could prevent AF recurrences in patients with persistent AF.

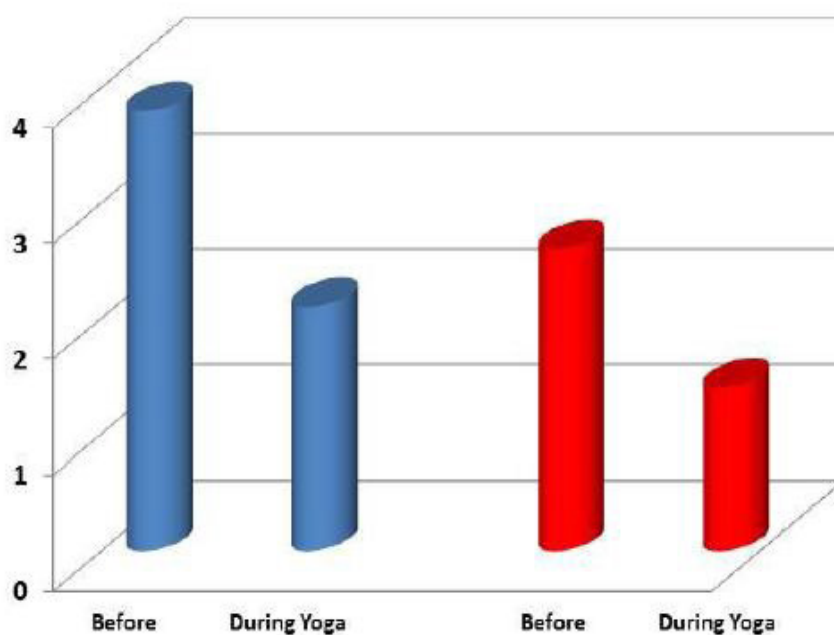
Unfortunately, our study does not allow us to infer the possibility that, in patients with early AF recurrence but already on antiarrhythmic drugs, acupuncture might exert an additive antiarrhythmic action. This possibility, however, was suggested by the results obtained in a more recent study in patients with paroxysmal AF.⁵⁰ Most of these patients were on propafenone, flecainide or amiodarone. Puncturing of the Neiguan spot resulted in a significant reduction of the arrhythmic burden that persisted during the whole follow-period. Even taking into account the small number of patients treated with acupuncture and the fact that only symptomatic episodes were measured, one could hypothesize that acupuncture could enhance the antiarrhythmic efficacy of these drugs by a combination effect on atrial electrical properties and autonomic mechanisms.

The possibility that acupuncture can be used in patients resistant to antiarrhythmic drugs to improve AF control requires, however, an adequate testing.

Yoga and Atrial Fibrillation

Regarding another ancient traditional eastern form of therapy and prevention, i.e., yoga, it has been recently shown that rigorous practice of yoga can help reduce episodes of atrial fibrillation and improve the symptoms of anxiety and depression often associated with this arrhythmia. According to a study recently presented in abstract form at the American College of Cardiology's 60th Annual Scientific Session (April 2011),⁵¹ intensive yoga training was capable of significantly reducing the episodes of atrial fibrillation. The study enrolled⁴⁹ patients with atrial fibrillation who had no physical limitations. During the first three-month control phase, participants were permitted to engage in any type of physical activity they were previously accustomed to doing. This was followed by a three-month study phase where patients participated in a supervised yoga program consisting of breathing exercises, yoga postures, meditation and relaxation. Forty-five minute yoga sessions were administered by a certified professional three times a week over the course of the study phase. Participants were also given an educational DVD and encouraged to practice the exercises at home on a daily basis depending on their comfort levels. All participants were new to the practice of yoga, and the program was designed to allow

Figure 2: Number of Total (left) and Phantom (right) AF Episodes Before and During Yoga Phase



beginners to progress safely from basic movements to more advanced practice over the course of the study. Episodes of irregular heartbeat were measured throughout the entire six-month study period using portable heart monitors and patient symptom log books. Participants were also asked to complete short self-administered surveys to assess anxiety, depression and quality of life scores during the control and study phases, and the differences were examined. Data showed the yoga intervention significantly reduced the number of episodes of irregular heart beat among atrial fibrillation patients during the study phase compared to the control phase where subjects were participating in the physical activity of their choice (3.8 ± 3 vs. 2.1 ± 2.6 , $p < 0.001$; Figure 2). Yoga also significantly reduced depression and anxiety scores and improved quality of life scores in the areas of physical functioning, general health, vitality, social functioning, and mental health.

Incoming Studies

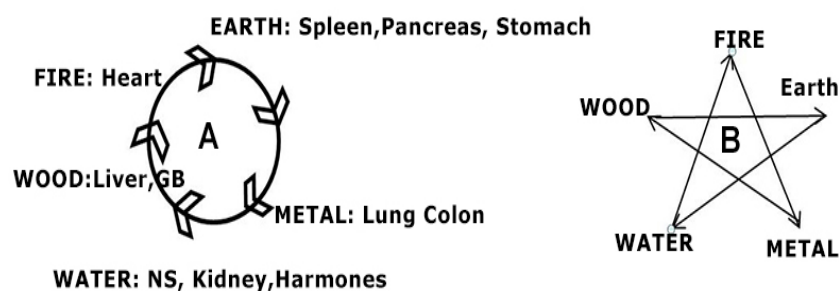
A randomized controlled study will soon start in Tuscany (Italy), and will take into consideration patients with non-valvular paroxysmal or persistent AF who received pharmacological or electric successful CV: the patients will be divided into two groups: the first group will be treated with standard antiarrhythmic pharmacological therapy, and the second with acupuncture and yoga or qigong.⁵² Results will be available in a two year period.

The “Five Elements Law” Of Traditional Chinese Medicine and Atrial Fibrillation

The Five Elements Law of Traditional Chinese Medicine is the basic foundation of pathophysiology and aetiology of illnesses in Far East medical doctrine.⁵³ Very briefly, it states that our organs and tissues are distributed in five “energetic fields”: Fire (heart), Earth (spleen, pancreas and stomach), Metal (Lung, Large Intestine), Water (Kidney, endocrine glands, nervous systems and urogenital organs) and Wood (Liver and Gallbladder) (Fig. 3)

The first rule of this Law says that an energetic field is never damaged by a contiguous field: Fire, for example, never damages Earth, or, in other words, Heart never damages Pancreas or Spleen, like Lung never damages Kidney, and so on. The second rule of the Law states that any field is able to damage a non-contiguous field: so, Fire is able to damage Metal (i.e., heart may cause a pulmonary edema and lung may provoke a chronic right-sided heart failure), Liver is able to damage Spleen (splenomegaly consequent to hepatic illnesses), and so on. Consequently, also atrial fibrillation could be related to the opposite fields of energy, i.e., Metal (Lung) and Water (Kidney, Endocrine organs and nervous system). And it is interesting a recent paper which considers atrial fibrillation caused by

Figure 3: The Law of Five Elements of ancient Traditional Chinese Medicine. A, first rule. B, second rule



lung surgery (Metal) related to elevation of the natriuretic peptide (Water). Moreover, an imbalance of vagal-sympathetic equilibrium (Water, because autonomic system is based on nervous tissue) may cause atrial fibrillation, both in case of elevation and reduction of vagal tone.

Conclusions

Recent reports suggest that acupuncture and yoga are safe, without any pro-arrhythmic effect and with limited cost. All these factors should be considered when evaluating the efficacy of therapeutic intervention for an epidemic disease as AF. Moreover, the practice of yoga is known to exert favourable effects on several risk factors for heart disease including high blood pressure, high cholesterol, hardening of the arteries, and stress and inflammation in the body. There are currently no proven complementary and non-invasive therapies that are known to decrease the symptoms of atrial fibrillation with minimal side effects and reasonable safety and efficacy.

Disclosures

No disclosures relevant to this article were made by the authors.

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