

Alternative medicine in atrial fibrillation treatment—Yoga, acupuncture, biofeedback and more

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Abstract: The last decade has seen a significant improvement in the management of atrial fibrillation (AF) with the development of newer medications and improvement in catheter ablation techniques. Recurrence of AF remains a significant problem in these patients and medications offer limited supportive role. Complementary and alternative treatment strategies therefore remain a viable option for these AF patients. Several studies have shown improvement in AF symptoms with yoga therapy, acupuncture and biofeedback. There are also several herbal medicine and supplements such as omega-3 fatty acids, antioxidant vitamins, barberry, motherwort, cinchona, Shensongyangxin, hawthorn, Kella and Wenxin Keli that have been evaluated as potential therapeutic options in AF. These studies are however limited by small sample sizes with mixed results. Besides the pharmacological action, metabolism, interactions with other medications and the adverse effects of the herbal medications and supplements remain poorly understood. In spite of the above limitations, complementary therapies remain a promising option in the management of AF and further studies are necessary to validate their safety and efficacy.

Keywords: Atrial fibrillation (AF) and alternative therapy; complementary therapy; yoga and AF

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Introduction

Atrial fibrillation (AF) is a common cardiac arrhythmia with a rapidly increasing prevalence. In 2010, the estimated prevalence in the United States alone was 5.5 million and is projected to increase three fold over the next 40 years (1,2). The common complications associated with AF are stroke, thromboembolism and cardiomyopathy. AF affects quality of life and also causes depression and anxiety (3,4). Current treatment strategies include rate control and rhythm control in addition to oral anticoagulation to mitigate stroke risk. Anti-arrhythmic drugs or catheter ablation can achieve rhythm control in AF. Recurrences of AF and adverse effects from the medications are the major limitations in

the management of AF. Several different alternative and complementary medicines have been tried for the treatment of AF. Besides, several different forms of herbal medications are popularly used in different cultures for the treatment of AF. In this review article we review the evidence supporting the use of these alternative and complementary medications in detail.

Alternative therapies

Yoga

Yoga is an ancient Indian science and is believed to promote general health and also has been shown to have a positive

impact in several chronic medical conditions (5-7). Yoga comprises of three key elements: asanas (body postures), pranayama (breathing exercises) and dhyana (meditation). This form of alternative therapy has been demonstrated to be beneficial in the treatment of several cardiovascular disorders. More recently, our group has shown that yoga therapy plays an adjunctive role in the treatment of AF in the “Yoga My Heart Study” (8). In our study, 52 patients with paroxysmal AF between the ages 18 and 80 years were enrolled and 49 of them completed the study. After practicing yoga for 60 minutes a day, thrice a week for 3 months, there was a decrease in symptomatic and symptomatic non-AF episodes (8). The mean number of symptomatic AF episodes decreased from 3.8 ± 3 to 2.1 ± 2.6 ($P < 0.001$), while the symptomatic non-AF episodes decreased from 2.9 ± 3.4 to 1.4 ± 2.0 ($P < 0.001$). There was also a decrease in heart rate and systolic blood pressure (8). Further, they observed an improvement in quality of life and decrease in anxiety and depression scores (8).

The benefits of yoga therapy in AF were thought to be due to modification of the autonomic nervous system activity at the hypothalamic-pituitary-adrenal axis level (8). The increase in parasympathetic activity is followed by a concomitant decrease in sympathetic activity, which results in lower resting heart rate and is also speculated to decrease the triggers for AF (8). Further, yoga could also decrease oxidative stress and inflammation and therefore was thought to play a role in down regulation of the atrial remodeling process (8). This therefore led to decreased symptoms of symptomatic AF and non-AF episodes. Given the above evidence, the impact of yoga on AF patients needs to be studied on a wider scale to assess its application in all AF patients.

Acupuncture

Acupuncture is an important part of traditional Chinese medicine. According to their doctrine, the art of acupuncture involves the belief that all humans have a form of vital energy called as Qi, which flows through channels called meridians linking all parts of the body (9). A total of 365 points are recognized, which are connected by 14 channels (or meridians) that run throughout the body through which the energy flow (Qi) can be reached and controlled (10). Diseased state or arrhythmias are believed to be due to the imbalance between Yin (normal heart) and Yang (abnormal heart) (11,12). The Neiguan spot is a spot in the area of Meridian of Minister of Heart, which is an area in the middle of the forearm between the tendons (13).

The Meridian of Minister of Heart is believed to control the heart rate and blood flow and therefore may play a role in controlling arrhythmias and this effect has been studied in a few studies.

Xu *et al.* studied the effectiveness of acupuncture for cardioversion of AF and atrial flutter (14). In this study, cardioversion was achieved in 85% of the patients with acupuncture compared to only 67.5% in the group of patients treated with amiodarone (14). Further, the duration to cardiovert was also shorter in the patients treated with acupuncture compared to amiodarone (14). Another study has suggested that acupuncture helps decrease recurrences of AF after cardioversion (12). The recurrence of AF after cardioversion with acupuncture was similar to the patients treated with amiodarone (12). Mechanistically, acupuncture at the Neiguan spot is thought to alter the sympathetic and parasympathetic balance and therefore appears to play a role in controlling AF. Studies evaluating the effect of acupuncture are limited by small sample sizes and studies evaluating the mechanism of action have not yielded consistent results (15). The limited evidence available points towards a beneficial role of acupuncture in the treatment of AF but needs further confirmatory evidence to be practiced on a wider scale.

Biofeedback

“Self regulation” therapies are a group of behavioral approaches that are used to help patients exercise voluntary control over various cardiovascular diseases. These therapies include muscle relaxation, self-hypnosis and various meditation methods. When the treatment includes use of monitoring device to record physiological process and help the patient control the physiological response, the method is called as “biofeedback”. Patients are engaged in goal directed activity that is designed to increase their skill and efficacy in reaching a physiological target through performance based biofeedback. Several different techniques are used in biofeedback like deep breathing, progressive muscle relaxation and guided imagery concentrating on particular color or image and meditation. During biofeedback session electrodes are attached to the skin. These electrodes send signals to a monitor, which displays sound, flash of light, or image that represent the heart rate or breathing. Different types of biofeedback are used to monitor different bodily functions.

Biofeedback increases the parasympathetic activity and thus can decrease heart rate. One of the successful methods of cardiovascular biofeedback is increasing

heart rate variability (HRV), which is an indication of autonomic nervous system activity. It is speculated that HRV biofeedback with paced breathing likely reinforces heart rate modulations by arterial baroreceptors, chemoreceptors, metabolic receptors and cardiopulmonary mechanoreceptors (16,17). HRV was shown to be a good predictor of survival in severe cardiovascular diseases (18). This approach can be used for the management of AF, especially to control ventricular rate. Biofeedback training was helpful in controlling ventricular rate as reported in a very small study (19,20). However this practice is yet to be adopted on a large scale and remains a viable option for patients with AF provided if they receive appropriate biofeedback training.

Complementary therapies

Omega-3 fatty acids

Polyunsaturated fatty acids have been shown to have a survival benefit in many cardiovascular conditions (21). The mortality benefit was due to a decrease in the incidence of arrhythmias (22). Because of these observations, the polyunsaturated fats have been evaluated extensively in several clinical studies for their potential benefits in the suppression of atrial arrhythmias. Several animal models suggested that the polyunsaturated fats decrease the excitability of the cardiomyocytes (23). The decreased excitability of the cardiomyocytes by the polyunsaturated fats is due to the inhibition of sodium and calcium channels and thereby prolonging the refractory period of the cardiac cells (24). The prolongation of the refractory period results in suppression of the spontaneous extrasystoles or triggers, which can initiate AF.

Multiple clinical trials have evaluated the benefit of these agents in suppressing AF recurrence with mixed results. Randomized clinical studies done by Nodari *et al.* and Kumar *et al.* clearly showed a decrease in AF recurrences after cardioversion (25,26). More recently the FORWARD trial, which was a randomized double blind study found no difference in AF suppression among patients taking polyunsaturated fatty acids and placebo (27). Further the most recent meta-analysis of published clinical trials evaluating the utility of polyunsaturated fats suggests that they are ineffective at suppressing both recurrent AF and post-operative AF (28). There was also no mortality benefit in patients with AF using these medications (28). Due to the clear lack of benefit as noted in the above observations, we

do not recommend the routine use of omega-3 fatty acids for complementing other AF therapies.

Vitamins and antioxidants

Oxidative stress is considered to play a pathogenetic role in AF and suppression of this oxidative stress may decrease arrhythmogenesis. Several different antioxidant agents such as vitamins C and E and N-acetylcysteine have been tried for the management of AF (29). A few studies have suggested that vitamins C and E decrease the risk of developing AF after cardiac surgery (30-33). Further, a few studies have shown that supplementation of vitamin C decreases the recurrence of AF after cardioversion and low vitamin E levels were an independent predictor of recurrence of AF (34,35). N-acetylcysteine is a scavenger of free radicals and the beneficial effect of this agent has been seen in the suppression of AF after heart surgery. Supplementation of this agent decreased the incidence of AF by 36-38% (36,37). The potential role of antioxidants such as probucol, xanthine oxidase inhibitors, nitric oxide donors and NADPH inhibitors are being studied in animal models to suppress AF (38-41). The initial studies evaluating the efficacy of these agents have shown mixed results and further evidence is needed to recommend them in the management of AF.

Herbal medicine and AF

Barberry (Berberis)

It is a shrub that belongs to the family Berberidaceae and contains around 500 species. This plant is a small shrub that commonly grows in the northeastern part of the United States, Central and Southern Europe and parts of Southeast Asia (42). The extracts from the fruits and roots of this plant have been used in Ayurvedic and Chinese medicine for the last 2,500 years (43). The active alkaloid extracted is called as berberine and is considered to have several medicinal properties (43,44).

This compound is also believed to affect the cardiovascular system and causes vasodilation, positive inotropic and negative chronotropic actions (45). In rat atrial myocytes, the berberine caused a dose dependent increase in the action potential duration (45). Further, this compound also caused an increase in contraction of the atrial myocytes (45). The biochemical action of this compound is believed to be mediated by means of inhibition of the transient outward potassium channel, thus prolonging the atrial refractory

period (45). Technically therefore it acts as a class IA or III anti-arrhythmic agent. However, the benefits of berberine in AF/atrial flutter have not been systematically studied in human clinical trials and therefore its acceptance in the treatment of AF remains very limited. Additionally it is also a potent inhibitor of CYP3A4 enzyme and many of the medications that are metabolized by these enzymes may reach dangerous levels and result in unwarranted adverse effects and needs to be cautiously used (46).

Shensongyangxin

This is a Chinese medication that has been used for the treatment of tachyarrhythmias (47). The major ingredients of this medication are ground beetle, dwarf lilyturf tuber, ginseng, tuber, Asiatic cornelian cherry fruit, danshen root, spine date seed, Chinese Taxillus herb and red peony root. Shensongyangxin inhibits sodium and calcium channels and thereby exerts its antiarrhythmic effects (48). In a recent, randomized, double blind multicenter study, Shensongyangxin and propafenone were found to have equal efficacy in the treatment of paroxysmal AF (49). The adverse effects from this medication were also low. This medication has also been used for the treatment of premature ventricular contractions and ventricular arrhythmias (50,51). This medication is approved for treating arrhythmias in China. Adequate caution needs to be exercised while using this agent because of the very limited evidence available with the use of this agent.

Cinchona

This plant belongs to the family of Rubiaceae. The bark of this plant contains several alkaloids namely quinine, quinidine, cinchonine and cinchonidine. The active ingredient of quinine is used for the treatment of malaria and night cramps, while quinidine is used for the treatment of AF and other cardiac arrhythmias. Quinidine exerts its anti-arrhythmic effect by means of inhibiting the sodium and potassium channels and is considered as a class IA anti-arrhythmic agent (52). It also has alpha receptor blocking properties and also inhibits the vagal output (52). Quinidine has been used for the treatment of AF; however, it has several unwanted side effects such as diarrhea, headache, tinnitus, thrombocytopenia and may cause torsades de pointes (53). The above adverse effects and availability of better anti-arrhythmic drugs limits the use of quinidine in the treatment of AF. The role of cinchona other than the purified form of quinidine on AF is unknown. However, since it contains the active ingredient quinidine, it still may

exert some degree of antiarrhythmic activity like quinidine. Besides it may also interact with other medications. Therefore patients should be cautioned against the routine use of cinchona extracts especially if they are taking other anti-arrhythmic drugs.

Hawthorn (*Crataegus oxycantha*)

Extracts from the flowers, leaves and berries of this plant are in use for a long time in the treatment of cardiovascular conditions (54). The extracts of this plant contain pharmacologically active flavonoids and procyanidines which exert various actions on the cardiovascular system (55). It is believed to prolong the action potential duration by inhibiting the delayed and inward rectifier potassium current thus causing negative chronotropic effect (56). Additionally it is also believed to inhibit the beta-adrenergic effects (55). It also has positive inotropic action which is exerted by inhibiting the Na-K ATPase activity and phosphodiesterase enzyme (55). The hydroalcoholic extracts of hawthorn have largely been used as a complementary therapy in heart failure treatment. The most commonly studied preparations of this compound are WS 1442 and LI 132 (57). Use of this compound resulted in improvement in exercise capacity and also decreased mortality in heart failure patients (58,59). Although it has class III anti-arrhythmic properties, its use in the management of atrial arrhythmias has not been systematically evaluated. Furthermore, it inhibits the biosynthesis of thromboxane A2 and may thereby increase the antithrombotic effect of antiplatelet agents and increase the risk of bleeding (60). There is some concern of interaction with digitalis through its effects on P-glycoprotein function; however, a large retrospective study did not find any evidence of major interaction with any drugs (61,62). In spite of its potential benefits, lack of clinical studies evaluating its use in AF precludes its use in the management of this condition. Patients should be cautioned against the use of this preparation if they are concomitantly using antiplatelet and or anticoagulant agents due to its potential for inhibiting thromboxane A2.

Motherwort (*Leonurus cardiaca*)

This is a medicinal plant belonging to the family Lamiaceae and is found across Europe, America and Asia. The extracts from this plant have been used in the treatment of several cardiovascular conditions such as arrhythmias, heart failure and other cardiac disorders (63). Several different bioactive compounds are found in the motherwort extract; lavandulifolioside, flavonoids, phenolic acids, iridoids, clerodane, furanolabdane, ursolic and oleanolic acids are

present in this extract besides several others (64). At an electrophysiologic level, the extracts of this plant cause inhibition of the inward calcium and potassium channels leading to prolongation of the cardiac cycle and activation recovery interval in the cardiac myocytes (63,64). This therefore can decrease the heart rate and has a potential benefit in the treatment of tachyarrhythmias such as AF. The action of the motherwort extract is considered to be similar to class III antiarrhythmic agents (63,64). In addition, this agent also decreases blood viscosity, fibrinogen volume and increases platelet aggregation (65). The active components of this preparation and its metabolism are unknown. Additionally at present there are no clinical studies evaluating the efficacy and safety of motherwort in the use of AF and for this reason this agent should not be routinely used. Further caution should be exercised with the use of this agent because of its potential interaction with platelets and fibrinogen, which may potentiate bleeding with anticoagulant agents.

Khella (Ammi Visnaga)

Khella is a small plant belonging to the family Apiaceae. This plant is native to Europe, Asia and Africa. The extracts from this plant was used for the treatment of angina symptoms. This extract also had anti-arrhythmic properties and eventually amiodarone was isolated from this extract. Therefore this plant product is also believed to have the same class III anti-arrhythmic action as amiodarone and also has a similar metabolic profile. However Khella as an agent for treatment of AF has not been systematically studied and therefore is not recommended for use in these patients.

Wenxin Keli

This is a Chinese herb and the extracts of this herb contains *Nardostachys chinensis* batil extract, *Codonopsis*, *notoginseng*, *amber*, and *rhizoma polygonati* (66). These compounds reportedly benefit patients with atrial arrhythmias and heart failure (66). The extracts from Wenxin Keli produced prolongation of the effective refractory period selectively in the atrial cardiomyocytes (66). Further, this increase in effective refractory period was rate dependent (66). The increase in effective refractory period was due to inhibition of the sodium channels and therefore can be considered a class I anti-arrhythmic agent. This agent also prevented the induction of persistent AF (66). A recent meta-analysis concluded that Wenxin Keli alone or in combination with other anti-arrhythmics decreases the recurrences of AF in patients with paroxysmal AF (67). Adverse effects

from Wenxin Keli were very few and included minor events such as nausea, vomiting, abdominal discomfort and sinus bradycardia (67). This agent appears to have novel properties, especially selective prolongation of the atrial effective refractory period and further rigorous studies are necessary to evaluate the efficacy and safety of this drug.

Others

There are several other traditional forms of medicine such as ayurveda, homeopathy and unani medicine that are very popular in several cultures. These forms of therapy are used for the treatment of chronic medical conditions such as arthritis, hypertension and cardiovascular conditions. But there have been no systematic studies evaluating these forms of therapy for the treatment of AF. Therefore patients should not undertake routine use of these forms of therapy for AF without seeking expert consultation. Besides, these medications may also interact with the regular medications used in the treatment of AF and therefore need to be cautiously used.

Conclusions

Complementary and alternative medicine treatments such as yoga and acupuncture are emerging as supportive strategies in the management of AF. Evidence is limited on the possible benefits of using herbal medicines and supplements in AF. Lack of randomized studies supporting the benefits of complementary and alternative treatments limits the acceptability of the results observed in smaller clinical studies and therefore the use of these treatment modalities in AF on a large scale. It is important for healthcare providers to be aware of the above strategies to provide their patients alternative treatments in patients who have recurrent symptoms and are intolerant to the current treatments. Additionally with increasing globalization, healthcare providers may encounter patients who may be taking these supplements and may need to provide them with the appropriate counseling regarding the use of these products.

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