REVIEW

Complementary and alternative medicine in the treatment of substance use disorders—a review of the evidence

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Abstract

Issues. Substance use disorders are chronic relapsing disorders, leading to significant impairment in psychosocial functioning. Conventional therapies have not been able to alter the outcome of these disorders significantly and frequent relapses continue to occur, despite the development of newer medications, like baclofen, ondansetron, etc. Hence, there is a need to look at complementary and alternate systems of medicine.

Approach. This article is a review of the evidence for complementary and alternate systems of medicine in substance use disorders. Articles were searched using the Medical Subject Headings (MeSH) database of the PubMed search engine and further non-indexed information was obtained from the Google search engine. The article is organised in parts, each reviewing a different system of medicine in the following order—alternate medical systems, biologically based therapies, energy-based interventions and mind–body interventions; as classified by the National Center for Complementary and Alternative Medicine, National Institutes of Health, USA.

Key Findings. The currently available evidence is limited and not very encouraging. At present only acupuncture, herbal therapies and mind–body interventions have shown some positive results in human trials and hold promise for the future.

Implications. This review emphasises the paucity of research into this important field especially the lack of rigorous human trials.

Conclusion. More systematic studies are required before these systems of medicine can be widely recommended in the treatment of substance use disorders. [Behere RV, Muralidharan K, Benegal V. Complementary and alternative medicine in the treatment of substance use disorders—a review of the evidence. Drug Alcohol Rev 2009;28:292–300]

Key words: substance use disorder, complementary medicine, energy-based therapy, mind–body intervention, biological therapy.

Introduction

Substance use disorders are chronic relapsing conditions, leading to significant morbidity and impairment in psychosocial functioning [1,2]. Management of substance use disorders has always been a challenge, with combinations of medications and psychosocial interventions being the mainstay of treatment. Advances in the understanding of the neurobiology of addiction have presented newer avenues in the medical management of substance use disorders. Established medications include disulfiram, acamprosate, naltrexone, opioid maintenance and nicotine replacement therapies [3,4]. Newer drugs like ondansetron, topiramate and baclofen have shown promise but more evidence still needs to be garnered regarding their efficacy [5–7]. Despite the changes in treatment modalities, treatment outcomes have not changed much and relapse is common [8,9].

The limitations of conventional therapies and an ongoing need for treatments with long-term efficacy in maintaining abstinence and preventing relapse to drug and alcohol abuse has resulted in attempts at using complementary and alternative systems of medicine in...
the management of these disorders. Even in developed countries like USA, a National Health Interview Survey in 2002 found that 62% of population use at least some form of alternative therapies [10]. This survey found that people preferred alternative medicine for reasons of ‘dissatisfaction with western medicine’, ‘personal control’ and ‘philosophical congruence’.

The National Center for Complementary and Alternative Medicine (NCCAM) [11] at the National Institutes of Health, USA, classifies complementary and alternative medicine (CAM) therapies into five major categories (NCCAM, National Institute of Health): (i) whole medical systems, for example, homeopathic and naturopathic medicine, Ayurveda or traditional Chinese medicine (acupuncture, acupressure); (ii) biologically based practices, such as use of herbs, special macronutrient diets, mega doses of vitamins, minerals and other dietary supplements; (iii) energy medicine which are of two types: (a) bioelectromagnetic-based therapies: these use energy fields including unconventional use of electromagnetic fields, for example, transcranial magnetic stimulation (TMS), transcranial direct current stimulation; and (b) Biofield therapies: these are intended to affect energy fields that purportedly surround and penetrate the human body. Therapies include qigong, Reiki and therapeutic touch; (iv) mind–body medicine, such as meditation, yoga, spiritual healing, art, music, therapy and biofeedback; and (v) manipulative and body-based practices, such as chiropractic or osteopathic manipulations, therapeutic massage.

Complementary and alternative medicines are interventions that by definition are not accepted by conventional practitioners, because they have not yet been shown to be effective clinically. Hence, there is a need to review the efficacy of these interventions before they can be widely recommended. This article is an attempt to review the alternative systems of medicine that are available for the treatment of substance use disorders and examine the evidence for their efficacy.

**Method**

The PubMed search engine was used to search articles, using the MeSH database search terms complementary therapies, homeopathy, ‘medicine, ayurvedic’, acupuncture, ‘Mind-Body and Relaxation Techniques’, yoga, TMS, biofeedback, ‘substance-related disorders’. Additional information from non-indexed sources was searched with the Google search engine.

Once retrieved, we have included all available articles. There were hardly any randomised controlled trials or methodologically rigorous studies to do a systematic review. The NCCAM classification structure is used to report the available results.

**Results**

**Whole medical systems**

*Ayurveda.* Ayurveda is the traditional and ancient system of Indian medicine. The classical Ayurvedic literature of ‘charaka samhita’ mentions the use of various medicinal wines to treat illnesses arising out of alcohol use.

A few Ayurvedic preparations have been tested in animal models for their impact on various substances. These include an Indian herbal brew known as *asavam* (SKV) [12] and BR-16A, [13–15] a multicomponent herbal preparation. The results are summarised in Table 1.

*Anticig.* An herbal formulation based on traditional Ayurvedic compositions has been introduced as an ‘anti-dote to the poisoning effects of tobacco and related products like cigarettes’ [16]. As well as being effective in tobacco cessation, the herbal nicotine-free pharmaceutical composition comprises an effective amount of sterilised dried plant powder/extracts obtained from *Ocimum sanctum*, *Myristica fragrans*, *Elettaria cardamomum*, *Syzygium aromaticum*, *Acorus calamus*, *Zingiber officinale*, *Cinnamomum zeylanicum*, and optionally with pharmaceutical additives to form solid dosage forms like tablets.

A single open trial using Anticig was carried out on 35 subjects [16]. The medication was prescribed ad libitum (one tablet of 500 mgs of the plant drug), one tablet as and when the subject desired to smoke. A total of 62% reportedly maintained abstinence after 8 weeks of use of the medication and 73% reported reduction in craving. Further evidence is currently not available.

*Homeopathy.* Homeopathy is a widely practiced system of medicine based on the principle of ‘like treats like’. Nux vomica & Hyoscyamus has been described for the treatment of alcohol-related withdrawal and delirium tremens. Extracts of strychnous nux-vomica has been found to reduce voluntary alcohol intake in rats [17]. A possible proposed mechanism of action is that the drug interacts with membrane aquaporins facilitating water influx into cells [18].

We did not come across any evidence for efficacy of these drugs in humans.

*Acupuncture.* In this system of medicine, life energy (called ‘qi’) is believed to flow throughout the body in specific channels, or ‘meridians’, ideally in a smooth, unobstructed and balanced cycle. Imbalances in this basic energy system eventually lead to disease. The metal acupuncture needles which are inserted at
<table>
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<th>Type of CAM therapy</th>
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<td>Anticig</td>
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<td>33 out of 35 subjects completed the treatment program of 8 weeks and 22 of these subjects were able to maintain complete abstinence by the end of 8 weeks.</td>
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<td>Acupuncture</td>
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<td>Margolin et al., 2002 [26]</td>
<td>RCT</td>
<td>Large single blind RCT on 620 cocaine-dependent patients. No significant difference found between groups at 6 month follow-up.</td>
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<tr>
<td>Bullock et al., 2002 [29]</td>
<td>RCT</td>
<td>Large, single blind, RCT on 503 alcohol-dependent patients. Acupuncture was not found to have any additional benefit over conventional treatment.</td>
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<td>Gates et al., 2006 [33]</td>
<td>Cochrane review</td>
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<td>Tian &amp; Krishnan, 2006 [34]</td>
<td>Pilot placebo controlled trial</td>
<td>Showed positive response of adjuvant acupressure to usual treatment</td>
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<td>Kudzu</td>
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<td>No significant differences in craving or abstinence rates between the two groups after a 1 month trial showed significant reduction in alcohol consumption in naturalistic setting.</td>
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<td>Lukas et al., 2005 [44]</td>
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<td>showed significant reduction in alcohol consumption in naturalistic setting.</td>
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<td>St John’s wort</td>
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<td>Salvia miltiorrhiza</td>
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<td>Magnesium</td>
<td>Margolin et al., 2003 [70]</td>
<td>RCT</td>
<td>Significant reduction in craving &amp; better abstinence rates in 18 methadone-maintained patients.</td>
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<td>Melatonin</td>
<td>Zhdanova &amp; Piotrovskaya, 2000 [74]; Garfinkel et al., 1999 [75]</td>
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<td>TMS</td>
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<td>rTMS over left dorso lateral prefrontal cortex (DLPFC) showed significant reduction in cigarette smoking without change in levels of craving.</td>
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<td>Camprodon et al., 2007 [79]</td>
<td>Open trial</td>
<td>rTMS over right DLPFC found to reduce craving in cocaine-dependent individuals 4 h later.</td>
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<td>EEG-Biofeedback</td>
<td>Scott et al., 2005 [88]</td>
<td>RCT</td>
<td>RCT on 120 patients of multiple substance dependence showed abstinence rate of 77% in test group at end of 1 year and significant improvement of tasks of variable attention.</td>
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<tr>
<td>Shafii et al., 1975 [90]</td>
<td>Open trial</td>
<td>54% discontinuation in consumption of hard liquor after 2–3 years practice of transcendental meditation.</td>
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<td>Yogas</td>
<td>Vedamurthachar et al., 2006 [92]</td>
<td>RCT</td>
<td>Sudarshan Kriya Yoga showed significant reduction in depression, ACTH and cortisol levels in 60 alcohol-dependent patients during a 2 week detoxification regime.</td>
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ACTH, adrenocorticotrophic hormone; EEG, electroencephalogram; RCT, randomised controlled trial; TMS, transcranial magnetic stimulation.
specific points in the body create a difference in electrical potential between inside and outside, thus stimulating extra cellular ion flow [19]. Auricular acupuncture is used in treatment of substance use disorders.

Acupuncture is believed to have an effect on monoamine systems. Recent evidence with animal experiments shows that it significantly reduces dopamine release in nucleus accumbens and normalises the mesolimbic dopaminergic system in rats sensitised to morphine [20] and alcohol [21]. Acupuncture might also reduce c-Fos like immunoreactivity by modulating post-synaptic neural activation in the striatum and nucleus accumbens [22].

Bullock et al. [23] conducted a controlled study on 40 patients. Both groups underwent an 8 week program of acupuncture in addition to attending AA meetings. Acupuncture was given at points specific for treatment of substance use disorders in patient group and at non-specific points for the control group. A total of 21 patients completed the acupuncture course and 12 of them maintained complete abstinence at 6 months, however, only 1 of the 40 controls had completed the 8 week course. Avants et al. [24] in a more recent study of 82 cocaine-dependent methadone-maintained patients found better abstinence rates with auricular acupuncture group as compared with needle insertion control condition or a no-needle relaxation control [24]. Acupuncture has also been found to ameliorate acute opioid withdrawal symptoms [25]. However, other clinical trials have found no significant differences between active acupuncture conditions and comparison conditions in reducing cocaine use [26] and reducing use of or craving for cocaine [27]. A randomised trial of electroacupuncture was not found to improve nicotine withdrawal symptoms [28]. Bullock et al. [29] in a large randomised, placebo-controlled single blind study on 503 alcohol patients did not find any additional benefit with acupuncture over conventional treatment. Trümpler et al. [30] in a pilot randomised controlled trial of laser, sham and needle auricular acupuncture failed to find any significant advantage for laser acupuncture. Various review articles have failed to confirm efficacy of acupuncture as a sole mode of treatment [31,32]. A recent Cochrane review [33] states that ‘There is currently no evidence that auricular acupuncture is effective for the treatment of cocaine dependence. The evidence is not of high quality and is inconclusive. Further randomized trials of auricular acupuncture may be justified.’

There is recent evidence that when used as an adjuvant, there is a positive response to the specific auricular acupuncture treatment on psychological distress, craving and drug/alcohol use measures [34]. Although there have been many studies of its potential usefulness, many of these studies provide equivocal results because of limitations of design, sample size and other factors like standardising the site for needle placement. The issue is further complicated by inherent difficulties in the use of appropriate controls, such as placebos and sham acupuncture groups [35]. The National Acupuncture Detoxification Association’s 5-point protocol [31] is an attempt at standardising the sites for needle placement in test and control groups for research purposes.

Biologically-based practices

Herbal medicines

Kudzu. Kudzu (Pueraria lobata) is one of the earliest medicinal plants used in traditional Chinese medicine. It has many profound pharmacological actions including anti-intoxication effects and antidipsotropic (anti-alcohol abuse) activity [36]. It has been examined in various animal and human studies for its efficacy in reducing alcohol consumption.

It has three isoflavonoids—daidzin, daidzein, puerarin [37,38]. Daidzin is a potent and selective inhibitor of human mitochondrial aldehyde dehydrogenase (ALDH-2). It is postulated that daidzin’s antidipsotropic effects are mediated by unknown physiological pathways catalysed by ALDH-2 different from that of the classical ALDH inhibitor disulfiram [37].

Animal studies have shown kudzu extracts reduce voluntary ethanol intake in Syrian golden hamsters [38] and rats [39–42]. Shebek et al. [43] conducted a randomised double-blind placebo-controlled clinical trial (n = 38, patients = 21, controls = 17) using twice daily dose of 1.2 gm of kudzu root extract. They failed to show any significant differences in craving or abstinence rates between the two groups after a 1 month trial. Lukas et al. [44] in a study where heavy alcohol users were treated with 25% concentration of the isoflavonoids for 7 days and then allowed to drink alcohol in a laboratory naturalistic setting, found that kudzu treatment resulted in significant reduction in the number of beers consumed and a decrease in the volume of each sip. These changes occurred in the absence of a significant effect on the urge to drink alcohol.

St John’s Wort. Hypericum perforatum is an herb native to Europe which has been widely studied for treatment of depression. Its constituents are Hyperforin, Hypercin, Flavonoids and Tannins [45]. The postulated mechanisms of actions have been increased striatal acetylcholine levels [46] inhibition of serotonin, norepinephrine and dopamine reuptake in hippocampus, hypothalamus and nucleus accumbens in rat brains and also neuronal inhibition by gamma-aminobutyric acid (GABA) [47,48].
Efficacy has been studied only in rat experiments in which it is found to reduce voluntary alcohol intake [49,50] and alcohol withdrawal symptoms [51]. No evidence is available for efficacy in humans.

**Tabernathe iboga.** It is a plant native to central Africa and is recognised to have potential in treating withdrawal as well as reducing craving for substances. Its constituents are ibogaine and its metabolite noribogaine. The postulated mechanism of action is that ibogaine causes up regulation of glial cell derived neurotrophic factor in the dopaminergic neurons in the ventral tegmental area which reduces alcohol consumption in rats. It has been found to reduce extra cellular levels of dopamine in the nucleus accumbens, and also to act as a mu-[52] and kappa-opioid receptor agonist, NMDA [53] and nicotinic receptor antagonist and also to block serotonin uptake [54] which might explain the effects of ibogaine on all substance use disorders.

Ibogaine’s ability to attenuate opioid withdrawal in the rat was first published by Dzoljic et al. [55]. It has also been shown subsequently to diminish morphine self-administration [56] cocaine self-administration [57], and to reduce alcohol consumption in rat models [58]. A synthetic analogue 18-methoxycoronaridine has been found to have effects similar to that of ibogaine in preclinical studies [59,60]. Many case series and open label studies have been reported regarding ibogaine’s efficacy in humans. Sheppard [61] described use of single dose of ibogaine 700–1200 mg in seven opioid-dependent subjects who reported significant decrease in withdrawal symptoms within 38 h. Alper et al. [62] conducted an open-label trial in 33 opioid-dependent subjects, 25 of which reported attenuated withdrawal symptoms after 24 h. Ibogaine has certain acute effects on administration, which include visual phenomenon described as a wakeful dream like state, ataxia, tachycardia and hypertension. Fatal cardiac arrhythmias have also been reported [63].

**Salvia miltiorrhiza.** This is also a traditional Chinese medicinal herb. It contains Miltirone [64] which has been found to inhibit up regulation of GABA-A receptor in rat hippocampal neurons during ethanol withdrawal [65]. Preclinical studies in rats show that intragastric administration of the active compound reduces voluntary ethanol intake [66,67], as compared with intraperitoneal administration suggesting an additional mechanism of inhibiting alcohol absorption [68].

**Biological supplementation**

Blum and colleagues have described [69] amino acid supplemenations with D & L isomers of phenylalanine and L-Tryptophan in doses of 500–1500 mg per day to reduce craving for alcohol, cannabis and nicotine as they are essential in synthesis of brain monoamines and endorphins.

Magnesium is an endogenous NMDA receptor blocker. Its supplementation in a randomised double-blind pilot study in 18 methadone-maintained patients was found to reduce craving and improve abstinence rates [70]. This preliminary finding needs to be confirmed in larger studies.

In animal models melatonin has been found to reduce alcohol intake [71] and reduce chronic ethanol-induced free radical damage and lipid peroxidation [72,73]. In human studies, melatonin has been found to reduce acute nicotine [74] and benzodiazepine [75] withdrawal effects.

**Energy medicine**

**Bioelectromagnetic-based therapies**

**Transcranial magnetic stimulation.** TMS is a method of inhibiting or activating neurons by external application of electromagnetic fields and is a useful non-invasive research tool to study cortical activity. There is some recent evidence for therapeutic implications in depression and auditory hallucinations. Using investigative TMS, it has been showed that alcohol [76] and chronic cocaine use [77] reduces excitability of the cortex. Preliminary studies on 14 patients using repetitive TMS of the left dorso lateral prefrontal cortex as a treatment method for nicotine dependence found significant reduction in cigarette smoking without change in levels of craving [78]. One session of 10 Hz repetitive TMS over right dorso lateral prefrontal cortex was found to reduce craving in cocaine-dependent individuals 4 h later [79].

**Biofield therapies**

Other energy-based therapies include qigong and therapeautic touch. Qigong is an ancient Chinese health practice which involves rhythmic body movements to balance the same energy ‘qi’ as described in acupuncture. There has been one study wherein 86 heroin addicts were randomised to a qigong group (n = 34), medication group (n = 26) receiving tapering dose of lofexidine or a control group (n = 26) receiving only symptomatic treatment for withdrawal symptoms. The Qigong group interestingly had urines negative for morphine by day 5 whereas the test was negative only by day 9 in the treatment group suggesting a role for qigong in detoxification of morphine dependence although the role of a placebo effect cannot be ruled out [80].
Mind body medicine

Electroencephalogram biofeedback

Electroencephalogram (EEG) biofeedback is a variation of the general principle of biofeedback where in the subject receives feedback on her/his physiological responses by which s/he learns to gain voluntary control over autonomic responses. Here EEG is used as an agent to provide feedback on brain wave patterns.

Studies on biological markers of alcoholism have found alcoholics and sons of alcoholics to have EEG wave patterns in the fast alpha (9–12 Hz) and beta (12–20 Hz) range [81–83]. Biofeedback aims at the patient learning to convert her/his brain wave activity from the alpha to theta range.

In an early case report [84] and an experimental study on 14 subjects, Saxby et al. [85] found alpha theta biofeedback reduced craving, depression and anxiety scores. Autogenic relaxation by biofeedback has been shown to develop internal locus of control in adolescents [86] and also has been proposed as an alternative treatment method for adolescents, especially those with stimulant abuse and attention and conduct problems [87]. In a recent randomised controlled study on 120 multiple substance abusers who received 50 sessions of biofeedback significant changes in the test of variable attention and Minnesota multiphasic personality inventory were found. Furthermore, at end of 1 year 77% in the test group were abstinent compared with 44% in the control group [88]. Methodological issues regarding the procedure and conduct of these studies have been raised [89]. However, these preliminary findings need to be replicated in larger randomised controlled trials.

Yoga, meditation and spirituality

Yoga and meditation have long been described for the treatment of substance use disorders. Shafii et al. [90] in a study on 216 patients practicing transcendental meditation found that 60% reported discontinuation of wine and beer consumption after 2–3 years of practice and 54% of subjects versus 1% of controls had stopped consumption of hard liquor. Gelderloos et al. [91] in a review of 24 studies on transcendental meditation found it to be an effective intervention which brought about in addition long-term changes in improved well-being, self-esteem and personal empowerment. The above studies, however, used self-report questionnaires on alcohol use by subjects and had no objective evidence for reduced substance use. An Indian study has found that Sudarshan Kriya Yoga, a form of yoga based on specific breathing techniques, significantly reduced depression scores on the Beck’s depression inventory and also serum adrenocorticotropic hormone, and cortisol levels in 60 alcohol-dependent patients undergoing a detoxification regime over a 2 week period [92].

A study on spirituality and mindfulness found spirituality scores negatively correlated with substance use whereas interestingly mindfulness scores were positively correlated with binge drinking patterns [93]. A comparison of faith-based versus traditional substance abuse treatment programs by Neff et al. [94] found that although both scored similarly on domains of ‘safe supportive environment, group activities and cohesion and role modeling’ they differed on domains of ‘spiritual beliefs and structure and discipline’.

Other mind–body interventions

A community-based rehabilitation program called ‘drumming out drugs’ has been evaluated by qualitative research method [95]. A component of group activities involving playing drums is added to rehabilitation programs. Interviews with participants indicate that it improves self-esteem and instils a feeling of being part of a community. A physiological mechanism proposed is that rhythmic auditory stimulation produces brain wave patterns in the theta range [96].

Manipulative and body-based practices

In a randomised control trial of 50 patients, massage therapy added as an adjunct to regular medical detoxification significantly reduced scores on the alcohol withdrawal scale in the early stages of the detoxification process in comparison to a ‘rest’ condition [97].

Conclusion

A number of alternative therapies are being tried in the treatment of substance use disorders. Although a few preliminary studies show encouraging results, none of the alternative therapies have significant evidence as of now. Of the evidence reviewed, acupuncture, EEG biofeedback and herbal therapies (kudzu, ibogaine) hold promise for the future. Mind body interventions, which are innocuous in nature and have shown efficacy in preliminary studies, warrant more attention. Studies of CAM face methodological difficulties relating to standardisation of procedures, provision of a control arm and blinding for double-blind randomised controlled trials. This review emphasises the paucity of research into this important field especially the lack of rigorous human trials.

The popularity of CAM, in the context of the limitations of traditional medicine is on the rise. Hence,
efforts to establish efficacy and standardised treatment procedures are warranted to make these interventions more effective.

References


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