REVIEW

Herbal remedies for anxiety – a systematic review of controlled clinical trials

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Received 2 November 2004; accepted 24 November 2004

Abstract

Anxiety is a prominent indication for herbal medicine. This systematic review was therefore aimed at summarising the evidence for or against the anxiolytic efficacy of such treatments. Six databases were searched for all randomised clinical trials testing herbal monopreparations in the alleviation of anxiety. Seven such studies and one systematic review were located. Eight different herbals were studied. The herbal medicines, which, according to these data are associated with anxiolytic activity in humans, are Piper methysticum and Bacopa monniera. Only for kava were independent replications available. It was concluded that there is a lack of rigorous studies in this area and that only kava has been shown beyond reasonable doubt to have anxiolytic effects in humans.

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Keywords: Herbal medicine; Phytomedicine; Anxiety; Efficacy; Systematic review

Introduction

Anxiety disorders, such as generalized anxiety, panic disorders, obsessive–compulsive disorder, phobias or post traumatic stress disorder, are common and a major cause of disability. Their 1-year prevalence figures are about 13% (Narrow et al., 1998). Anxiety is also an important component of many other psychiatric or medical conditions (Lavie and Milani, 2004). Effective treatments such as anxiolytic drug therapy or cognitive-behavioural therapy exist (Sadock and Sadock, 2000) but, many patients remain untreated, experience adverse effects of benzodiazepines (Woods et al., 1987), or do not benefit from full symptom control (Issakidis and Andrews, 2002).

It has been estimated that 43% of anxiety sufferers use some form of complementary therapy (Eisenberg et al., 1998). The most popular treatments include herbal medicines (Astin, 1998). Similarly, anxiety disorders are amongst the most common reason for people to try herbal medicines (Wong et al., 1998). The aim of this systematic review is therefore to summarise the evidence for or against the effectiveness of herbal medicines for these indications.

Methods

Electronic literature searches were conducted using the following databases: AMED, Cinahl, Embase, Medline, PsychInfo and PubMed (all from inception to August 2004). The terms used for the electronic searches were limited to clinical trial, randomised/
controlled trial, herbal medicine, remedy, etc, phytotherapy, phytomedicine, anxiety, stress, panic disorder, obsessive–compulsive disorder, phobia. Further researches were conducted by hand-searching departmental files as well as a range of complementary medicine journals, and by asking experts in this field. Finally, several manufacturers of herbal medicines were asked to contribute articles of relevance. No restrictions on language of publications were applied.

Only trials with oral medication of herbal medicines were included and other routes of administration such as inhalation or topical application (aromatherapy) were excluded e.g. (Graham et al., 2003). St. John’s wort (Hypericum perforatum) was not included in this review as it is primarily an antidepressant rather than an anxiolytic remedy. Clinical trials of preparations containing more than one herbal remedy were excluded e.g. (Hanus et al., 2004; Gopinathan et al., 1999; Mills et al., 2002; Kohnen and Oswald, 1992) and so were herbal medicines with psychedelic activity e.g. (Riba et al., 2001) or duplicate publications e.g. (Kohnen and Oswald, 1988). Studies of anxiety related to specific conditions such as HIV infection (Weber, 1999) or depression (Lenoir et al., 1999) were also excluded.

All articles thus retrieved were read in full by the author. Data were evaluated and validated according to pre-defined criteria.

**Results**

Seven RCTs and one systematic review were located with the above search strategy (Akhondzadeh et al., 2001; Andreatini et al., 2002; Bradwejn et al., 2000; Galduroz and Carlini Ede, 1994; Leite et al., 1986; Pittler and Ernst, 2002; Stough et al., 2001; Wolfson and Hoffmann, 2003). They relate to eight herbal medicines.

**Blue skullcap (Scutellaria lateriflora)**

Wolfson and Hoffman conducted a double-blind, placebo-controlled cross-over trial with 19 healthy volunteers (Wolfson et al., 2003). They took single doses of a placebo, a 350 mg capsule of freeze dried Scutellaria lateriflora, a 100 mg capsule of the same or 200 mg of the same. Anxiety was quantified via a visual analogue scale. The results suggested that the two higher doses generated a reduction in anxiety 60 min after administration. Even though these findings seem promising, the study has several important limitations, most importantly it only used descriptive statistics for evaluation of the data. It is thus not possible to tell whether the changes were statistically significant or reflected merely a numerical trend.

**Gotu kola (Centella asiatica)**

A small ($n = 40$) double-blind RCT tested the efficacy of gotu kola on anxiety symptoms in healthy volunteers (Bradwejn et al., 2000). Volunteers took either a single oral dose of 12 g gotu kola or placebo. Compared to placebo, the acoustic startle response was diminished 60 and 90 min after the administration of one dose of gotu kola. No changes in self-rated anxiety were noted in this single-dose study. These results are preliminary by nature and require confirmation in larger studies.

**Guarana (Paullinia cupana)**

In a small and poorly reported RCT, 30 healthy volunteers were given either guarana extract, caffeine or placebo (Galduroz et al., 1994). No significant effects on anxiety were noted.

**Kava (Piper methysticum)**

A Cochrane review included 11 placebo-controlled RCTs of kava mono-preparations as a treatment of anxiety (Pittler et al., 2002). Six of these studies could be submitted to a meta-analysis where the Hamilton Anxiety Scale was the common outcome measure. Its results show a significant reduction of anxiety relative to placebo. The weighted mean difference was 5.0 (95% CI = 1.1 – 8.8). The adverse effects reported in these studies were mild, transient and infrequent.

**Keenmind (Bacopa monniera)**

Stough et al. randomised healthy volunteers to receive either 300 mg Bacopa monniera extract or placebo for 12 weeks (Stough et al., 2001). The results show a reduction in state anxiety in the experimental compared to the control group. The effects were more marked at 12 compared to 5 weeks of treatment.

**Lemon grass (Cymbopogon citratus)**

A placebo-controlled, double-blind RCT of Lemon grass extract included 18 patients suffering from trait anxiety (Leite et al., 1986). The extract was administered as a single dose of abafado (Brazilian lemon grass tea), and its effects were quantified 30 min later under the stress of a cognitive test. The results revealed no significant inter-group differences to suggest an anxiolytic effect.

**Passion flower (Passiflora incarnata)**

In a double-blind RCT, 32 patients with generalised anxiety disorder were randomised to receive 45 drops of
a passionflower tincture or 30 mg oxazepam per day (Akhondzadeh et al., 2001). After 4 days of treatment, no significant differences in terms of anxiety levels were noted. Patients treated with passionflower reported fewer adverse effects than those receiving the synthetic anxiolytic. Even though the authors conclude that passiflora is effective, the results require cautious interpretation: the trial was not designed as an equivalence study and conclusions about equivalent efficacy cannot be drawn.

Valerian (*Valeriana officinalis*)

In a double-blind RCT, 36 patients with generalised anxiety disorder were randomised to receive either 50–150 mg valerian extract per day or 2.5–7.5 mg diazepam or placebo (Andreatini et al., 2002). All three groups showed marked decreases in doctor- and self-rated anxiety at the end of the treatment phase. There were no significant differences between the groups. It seems unclear whether this is due to the absence of an effect or due to a type II error because of the very small sample size.

Discussion

Considering that anxiety is a frequent indication for herbal medicine, the paucity of RCTs in this area is perhaps the most remarkable finding of this systematic review. Similarly impressive is the fact that, for the majority of herbal treatments supported by RCTs, independent replications are missing. The only herbal anxiolytic, which has more than one RCT to its credit is kava. Sadly kava has been banned, in many countries, due to a suspicion that it may cause liver damage (Ernst, 2004).

Several of the RCTs were burdened with poor reporting, methodological flaws or both. Future research in this area should make sure it overcomes these obstacles. In particular, sufficiently large sample sizes, longer follow-up period, intention to treat analyses and full characterisation of the herbal medicine employed are required.

Apart from kava which has been repeatedly shown to be as effective as benzodiazepines, none of the herbal medicines reviewed here are associated with an effect size comparable to standard anxiolytic treatments (Gould et al., 1997). In essence, this suggests that, within the realm of herbal medicine, there are currently no well-documented alternatives to conventional anxiolytic therapies.

The present review has several limitations. As with all such projects it is possible that not all relevant RCTs were found. It is also conceivable that those which were found are the ones that tended to be associated with positive results. In this are, publication bias could be a particularly important potential confounder (Ernst and Pittler, 1997). A further limitation is the fact that many RCTs have significant flaws, a circumstance which prevents any firm conclusions.

In conclusion, few rigorous trials of herbal anxiolytics are currently available. Apart from kava, none has been shown beyond reasonable doubt to be efficacious.

References


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