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Short communication

Is lavender an anxiolytic drug? A systematic review of randomised clinical trials

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ABSTRACT

Background: Lavender (*Lavandula angustifolia*) is often recommended for stress/anxiety relief and believed to possess anxiolytic effects.
Aim: To critically evaluate the efficacy/effectiveness of lavender for the reduction of stress/anxiety.
Methods: Seven electronic databases were searched to identify all relevant studies. All methods of lavender administration were included. Data extraction and the assessment of the methodological quality of all included trials were conducted by two independent reviewers.
Results: Fifteen RCTs met the inclusion criteria. Two trials scored 4 points on the 5-point Jadad scale, the remaining 13 scored two or less. Results from seven trials appeared to favour lavender over controls for at least one relevant outcome.
Conclusion: Methodological issues limit the extent to which any conclusions can be drawn regarding the efficacy/effectiveness of lavender. The best evidence suggests that oral lavender supplements may have some therapeutic effects. However, further independent replications are needed before firm conclusions can be drawn.

Introduction

Lavender (*Lavandula angustifolia*) has a long history of medicinal use and is purported to possess anxiolytic, sedative and calming properties (Cavanagh and Wilkinson 2002). Most commonly it is recommended for oral administration. More recently, lavender is also being employed in aromatherapy (Setzer 2009) although specific pharmacological effects of lavender aromatherapy are difficult to distinguish from any innate or learned preferences to this, or any other, odour (Bradley et al. 2009).

The chemical composition of lavender is complex and several of its constituents (e.g. linalool and linalyl acetate) have been proposed as being responsible for the perceived anxiolytic effects (Setzer 2009). In animal models, linalool has been found to inhibit GABA(A) binding reception in the CNS inducing a relaxed state (Brum et al. 2001; Hossain et al. 2004). Until recently, this activity had not been noted in human studies.

Anxiety is a common disorder (14% of the EU population suffer from one or more anxiety disorders each year (Wittchen et al. 2011)) but can be severe and debilitating, often requiring medication. Lavender may provide a gentler treatment option than conventional anxiolytic drugs. Apart from rare allergic reactions (Coulson and Khan 1999) and gastrointestinal complaints (after excessive intake) (Leung and Foster 1996), lavender intake seems to be reasonably safe.

This systematic review is aimed at critically evaluating the data from randomised clinical trials (RCTs) of all types of lavender preparations (oral, olfactory, topical) for the treatment of anxiety.

Methods

The following electronic databases were searched from their inception up to December 2010: Medline, EMBASE and PsychInfo (via OVID), AMED and CINAHL (via EBSCO), The Cochrane Library, and ISI Web of Knowledge. The search terms used included *lavender*, and *anxiety or stress*, and derivatives of these terms (see Appendix A for electronic search strategy). Our own departmental files and the reference lists of all selected articles were searched for further relevant studies.

Articles were included if they reported an RCT in which human subjects with or without clinical anxiety were treated with any type of lavender preparation (excluding those containing other ingredients (e.g. Corner et al. 1995; Graham et al. 2003; Nord and Belew 2009)) and which reported validated measures of anxiety or stress as an endpoint (e.g. State Trait Anxiety Inventory; STAI, Hamilton Anxiety and Depression; HAD), standardised measures of anxiety (e.g. visual analogue scales were acceptable) or physiological measures of stress (e.g. salivary levels of cortisol, heart rate, galvanic skin response). We excluded studies that were not randomised (e.g. Willman et al. 2009) along with studies comparing two different forms of lavender treatments without a control condition, those

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comparing a combined lavender treatment against a no-treatment control (e.g. Hoya et al. 2008), uncontrolled trials and those in which no clinical data were reported (e.g. Buckle 1993; Motomura et al. 1999). No language restrictions were imposed. Hard copies of all articles were obtained and read in full by two authors (RP, RT).

Data from the articles were independently extracted from all included studies by two reviewers (RP, RT) according to pre-defined criteria (Tables 1 and 2). We only reported between-group analyses from outcomes that conform to our inclusion criteria above. To assess methodological quality, the Jadad scale[1] was used (Jadad et al. 1996). To supplement the Jadad score, using Verhagen et al. (1998) and Boutron et al. (2005) as a guide, additional information pertaining to risk of bias was extracted (Table 2). Discrepancies were resolved through discussion between the authors. A meta-analysis was considered but deemed to be not appropriate because of the clinical and statistical heterogeneity of the primary studies.

Results

The literature search identified 440 potentially relevant titles and abstracts. Fifteen RCTs involving 1565 participants met the inclusion criteria (Fig. 1). Where possible, between-group analyses of the main anxiety outcomes are presented in Table 1. The included studies were published between 1995 and 2010, originated from six countries and were all written in English. Sample sizes ranged from 16 to 340. The majority of trials used *Lavandula angustifolia* unless otherwise stated.

Eight trials (Bradley et al. 2009; Howard and Hughes 2008; Kutlu et al. 2008; Morris 2002; Motomura et al. 2001; Sgoutas-Emch et al. 2001; Toda and Morimoto 2008; Xu et al. 2008) used healthy volunteers with assumed normal levels of anxiety in which anxiety was induced for the purpose of the study. One trial (Soden et al. 2004) assessed the efficacy of lavender in cancer patients with high levels of anxiety and depression. Three studies (Braden et al. 2009; Kritsidima et al. 2010; Muzzarelli et al. 2006) looked at pre-procedural anxiety (e.g., dental appointment, gastrointestinal endoscopic procedure, pre-operation). One trial (Dunn et al. 1995) involved patients in an Intensive Care Unit (ICU) and two studies focussed upon the value of lavender for individuals with generalised or sub-syndromal anxiety disorder (according to DSMIV or ICD-10) (Kasper et al. 2010; Woelk and Schlafke 2010).

The methodological quality of the included trials was variable but generally poor (Table 2); Jadad scores ranged from 0 to 4, with just two trials (Kasper et al. 2010; Woelk and Schlafke 2010) achieving a score of 4 points. The majority of trials scored less than 2.

Different methods of lavender administration were tested. Eight trials (Braden et al. 2009; Howard and Hughes 2008; Kritsidima et al. 2010; Kutlu et al. 2008; Motomura et al. 2001; Muzzarelli et al. 2006; Sgoutas-Emch et al. 2001; Toda and Morimoto 2008) assessed the efficacy of lavender aromatherapy. Two trials (Dunn et al. 1995; Soden et al. 2004) employed aromatherapy massage, one used an oil-dripping technique (Xu et al. 2008), one involved bathing in lavender oil (Morris 2002) and three used oral capsules (Bradley et al. 2009; Kasper et al. 2010; Woelk and Schlafke 2010). The results of the 15 trials will be described in more detail in the following section, according to the method of administration.

Inhalation of lavender

Eight trials (Braden et al. 2009; Howard and Hughes 2008; Kritsidima et al. 2010; Kutlu et al. 2008; Motomura et al. 2001; Muzzarelli et al. 2006; Sgoutas-Emch et al. 2001; Toda and Morimoto 2008) investigated the effect of lavender oil inhalation. Four trials (Braden et al. 2009; Kritsidima et al. 2010; Kutlu et al. 2008; Motomura et al. 2001) reported a significantly positive effect for at least one anxiety outcome measure. Kritsidima et al. (2010) compared lavender oil aromatherapy with no oil (using a candle burner) for patients waiting for a dental appointment. They found a significantly greater reduction in State Trait Anxiety Inventory (STAI) compared to the control group ($p < 0.001$) but no significant between-groups difference in the Modified Dental Anxiety Scale (MDAS). Braden (Braden et al. 2009) found a lavender aromatherapy group (lavender hybrid) had significantly less self-reported anxiety than either control group ($p < 0.01$) for pre-operative anxiety.

Both Motomura et al. (2001) Kutlu et al. (2008) induced stressful situations in healthy volunteers. Lavender odour was released in the experimental conditions but not the control conditions. Motomura et al. (1999) found that anxiety levels were associated with reduced mental stress in the lavender condition although no significant differences between conditions were found for physiological measures. Kutlu et al. (2008) used an exam to induce anxiety and found the lavender group had significantly lower anxiety scores on the STAI than the control group ($p < 0.001$) after the 60-min exam. Unfortunately as baseline anxiety scores would be likely to be very high prior to an exam, baseline anxiety scores were not taken, so it is impossible to establish change over time. Both trials suffer major methodological issues (Table 2).

Four inhalation trials (Howard and Hughes 2008; Muzzarelli et al. 2006; Sgoutas-Emch et al. 2001; Toda and Morimoto 2008) did not demonstrate an effect. Muzzarelli et al. (2006) used patients waiting for an gastrointestinal endoscopy. Reductions in within-group anxiety levels were reported in both the lavender (Provencal lavender) and grapeseed inhalation groups, however, no between-group analyses were performed which limits its conclusiveness. Longer inhalation time (more than 5 min) was suggested for future trials.

The remaining trials (Howard and Hughes 2008; Sgoutas-Emch et al. 2001; Toda and Morimoto 2008) of lavender inhalation assessed efficacy in healthy volunteers. Stress was induced in a variety of ways e.g. arithmetic tasks (Sgoutas-Emch et al. 2001; Toda and Morimoto 2008) and an arousal task (Howard and Hughes 2008). In Toda's (Toda and Morimoto 2008) study it was found that during the experimental period, neither group showed any significant variation in levels of salivary cortisol (stress hormone). In the lavender group, levels of chromogranin A (CgA is a novel stress marker found in saliva (Nakane et al. 1998, 2002)) that had been elevated at the end of the arithmetic task were statistically lower 10 min later whereas they were still elevated in the control group. However, there was no significant difference between the groups at 5 and 10 min implying that lavender may only help stress levels to drop quicker. There were no significant between group differences in subjective ratings of stress.

Sgoutas-Emch et al. (2001) compared four groups; two received lavender aromatherapy and two groups did not receive aromatherapy. One group from each condition knew about their group allocation, whilst the two other groups did not. The aim was to see if knowledge of treatment impacted on results. In fact, no significant differences between the four groups were found on any measure. Interestingly, Group 3 had significantly higher levels of anxiety prior to task than other three groups yet this group's anxiety levels went down following the arousal task. In general, the authors felt a more stress-provoking task might be required in future trials.

Howard and Hughes (2008) employed an experimental stress task to compare lavender with tea tree oil odour (against a no odour condition) in an attempt to compensate for previous experiments that do not test lavender against another strong odour. They also

[1] Jadad score (1 for randomisation, 1 for sequence generation and allocation concealment, 1 for stating it is double blind and 1 for description of blinding and appropriateness and 1 for withdrawal stating number and reasons per group).