Homeopathy (2006) 95, 151–162

doi:10.1016/j.homp.2006.05.005, available online at http://www.sciencedirect.com

EDUCATION AND DEBATE

Homeopathy for anxiety and anxiety disorders: A systematic review of the research

K Pilkington[1,*], G Kirkwood[2], H Rampes[3], P Fisher[4] and J Richardson[5]

[1]*School of Integrated Health, University of Westminster, London, UK and Research Council for Complementary Medicine, London, UK*
[2]*Research Council for Complementary Medicine, London, UK*
[3]*Barnet, Enfield and Haringey Mental Health NHS Trust, Northwest Community Mental Health Team, Edgware, Middlesex, UK*
[4]*Royal London Homoeopathic Hospital, London, UK*
[5]*Faculty of Health and Social Work, University of Plymouth, Devon, UK and Research Council for Complementary Medicine, London, UK*

Objective: **To conduct a systematic review of the clinical research evidence on homeopathy in the treatment of anxiety and anxiety disorders.**
Methods: **A comprehensive search of major biomedical databases: MEDLINE, EMBASE, CINAHL, PsycINFO, Cochrane Library; and of specialist complementary and alternative medicine (CAM) databases: AMED, CISCOM and Hom-Inform was conducted. Efforts were made to identify unpublished and ongoing research using relevant sources and experts in the field. Relevant research was categorised by study type and appraised according to study design. Clinical commentaries were obtained for studies reporting clinical outcomes.**
Results: **Eight randomised controlled studies were identified. The types of anxiety and anxiety disorders studied were test anxiety, generalised anxiety disorder and anxiety related to medical or physical conditions such as cancer or surgical procedures. Single case reports/studies were the most frequently encountered study type but other study types including uncontrolled trials/case series and surveys were also found. No relevant qualitative research was identified.**
Conclusions: **A comprehensive search demonstrates that the evidence on the benefit of homeopathy in anxiety and anxiety disorders is limited. A number of studies of homeopathy in such conditions were located but the randomised controlled trials report contradictory results, are underpowered or provide insufficient details of methodology. Several uncontrolled and observational studies reported positive results including high levels of patient satisfaction but because of the lack of a control group, it is difficult to assess the extent to which any response is due to homeopathy. Adverse effects reported appear limited to 'remedy reactions' and included temporary worsening of symptoms and reappearance of old symptoms.**
On the basis of this review it is not possible to draw firm conclusions on the efficacy or effectiveness of homeopathy for anxiety. However, surveys suggest that homeopathy is quite frequently used by people suffering from anxiety. If shown to be effective, it is possible that homeopathy may have benefits in terms of adverse effects and

*Correspondence: K Pilkington, School of Integrated Health, University of Westminster, 115 New Cavendish Street, London W1W 6UW, UK
E-mail: k.pilkington@westminster.ac.uk
Received 21 December 2005; revised 30 January 2006; accepted 8 May 2006

acceptability to patients. Consequently, further investigation is indicated. Future research should be of pragmatic design and include qualitative studies. *Homeopathy* (2006) **95**, 151–162.

Keywords: homeopathy; anxiety; anxiety disorders; systematic review

Introduction

Anxiety has been defined as a 'persistent feeling of dread, apprehension and impending disaster or tension and uneasiness'.[1] The term anxiety disorders is used as an umbrella term for a number of conditions including panic disorder, phobias, obsessive–compulsive disorder, generalised anxiety, post-traumatic stress disorder and anxiety disorder due to a general medical condition. Severe anxiety can affect the individual's ability to carry out the activities of normal life and in individuals with generalised anxiety disorder, symptoms may last for months and recur regularly, and are often worsened by stressful events.[2] Reported prevalence in the UK in 2000 was: mixed anxiety and depressive disorder 88/1000, generalised anxiety disorder 44/1000, all phobias 18/1000, obsessive–compulsive disorder 11/1000 and panic disorder 7/1000.[3] A range of therapeutic approaches are available but patients may turn to complementary therapies due to adverse effects of medication, time and effort associated with non-pharmacological therapies, lack of response or simply preference for the complementary approach.

Anxiety and other mental health problems such as depression and insomnia are amongst the most common reasons for individuals to seek treatment with complementary therapies, including homeopathy. Eisenberg *et al*[4] reported that 42.7% of adults with anxiety in the US had used complementary therapies in the previous year. A high rate of use of complementary therapies in the USA among adults who met criteria for common psychiatric disorders was reported by Unutzer *et al*[5]; respondents with panic disorder were particularly likely to report use. Davidson and colleagues[6] found that, overall, 25.3% of cohorts of patients in the UK and USA attending homeopathic centres met the criteria for at least one anxiety disorder. A survey of homeopathic general practitioners in France demonstrated that stress and anxiety was one of the most common reasons for consultation.[7]

In the UK, a survey of complementary and alternative medicine (CAM) organisations sought to discover which therapies were thought to be suited to which medical conditions. Stress and anxiety was one of the seven conditions most frequently cited as suitable for treatment with a complementary therapy, although homeopathy was not specifically mentioned.[8]

Popular self-help literature recommends the use of homeopathy for anxiety. For example the homeopathic medicines *Arsenicum album*, *Calcarea carbonica* and *Lycopodium clavatum* are recommended for anxiety and associated disorders in a book on homeopathy aimed at the general public[9] while *Aconite*, *Argentum nitricum*, *Arsenicum album*, *Calcarea carbonica* and *Ignatia amara* are suggested for anxiety in a book on integrated medicine intended for a similar audience.[10]

Homeopathy

Homeopathy is among the most popular of CAM therapies; lifetime use by the UK population was estimated at 5.7% in 1998[11] and sales have increased 12–13% annually since then.[12] Several systematic reviews and meta-analyses have appraised evidence of the efficacy of homeopathy in a range of conditions.[13–15] In each case, the evidence appears positive overall for homeopathy in relation to placebo but inconclusive for specific conditions. A more recent meta-analysis came to a negative conclusion, but was based on only eight studies (of the 110 initially located), none of which investigated use of homeopathy in anxiety.[16]

The wide use of homeopathy, particularly in continental Europe, together with interest in homeopathy as a treatment for psychological conditions[17–19] suggested that a review of the evidence in anxiety and anxiety disorders would be valuable.

Methods

Search strategy

A comprehensive search for clinical research was carried out on a range of general health and specialist databases. Citations were sought from relevant reviews and relevant websites were also included in the search, including those of MIND and the Mental Health Foundation.

Databases searched

General databases: CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), EMBASE, MEDLINE (and PubMed) and PsycINFO. Specialist CAM databases: AMED, CISCOM, Cochrane Complementary Medicine Field Registry, Hom-Inform.

Search terms

The basic search terms for homeopathy included exp homeopathy or exp homeopathic drugs or homoeop* or homeop* while those for anxiety included exp

anxiety or exp anxiety disorders or anxiety. Search strategies were adapted for each of the databases searched and the following additional terms used for specific databases where necessary:

anx* or agoraph* or obsessive compulsive or obsessive–compulsive or panic or phobic or combat disorders or stress disorders.

Efforts were made to identify unpublished and ongoing research using relevant databases such as the National Research Register (UK) and Clinicaltrials.gov (US) together with experts in the field. Searches of databases were conducted in January and February 2004 and searches for unpublished studies carried out in May 2004. Searches were repeated in 2005, for studies published up-to the end of August 2005.

Filtering

Potential research articles were noted for retrieval and given a preliminary 'study type' categorisation according to a flow-chart system developed for this project. The basic categories included systematic reviews, randomised controlled trials, controlled clinical trials, uncontrolled studies, case reports, qualitative studies and surveys. Animal research and basic laboratory-based research were not included. Two reviewers carried out this process independently, notes were compared and in cases of disagreement the original articles were retrieved.

Selection criteria

Types of studies: Initially all clinical studies were identified. The main focus of this review is evidence provided by controlled studies. However, other studies such as uncontrolled and observational studies were also included if the effect on anxiety was reported as a clearly defined outcome. Attempts were also made to locate relevant qualitative studies.

Types of participants: participants with anxiety or an anxiety disorder.

Types of intervention: homeopathy (individualised or complex).

Types of outcome measures: rating scales and patient-focused measures such as satisfaction where relevant.

No language restrictions were imposed. A translation was obtained for potentially relevant studies that were only available in languages other than English.

Data collection and analysis

Data was extracted systematically using a specifically designed form. Data extracted included details of selection criteria and procedure, the participants, the intervention and any comparison or control intervention, aspects of the methodology and outcome measures and results. Clinical trials were appraised using a standardised appraisal framework specifically developed for this project and based on criteria recommended in the Centre for Reviews and Dissemination.[20] Criteria included method of randomisation, allocation concealment and level of blinding (if relevant), dealing with missing values, withdrawals and dropouts, measures of compliance and outcomes. For each study, two researchers (KP, GK) conducted data extraction and appraisal independently and any disagreements or discrepancies were resolved by discussion. Where consensus could not be obtained or further details from a translation required, a third reviewer was consulted.

Clinical commentaries

A clinician with relevant training and experience (HR or PF) was asked to comment on each study focusing on clinical relevance and practical issues. Commentary frameworks were specifically developed for this project and incorporate a number of closed and open questions with space for further comments. Summaries of the commentaries are provided in the tables.

Main results

Systematic reviews:

No systematic reviews focusing solely on the topic of homeopathy for anxiety/anxiety disorders were identified. A systematic review of complementary and self-help treatments for anxiety disorders published in 2004 included homeopathy as one of the interventions.[21] The authors concluded that, based on the results of the two trials included, there was no convincing evidence of effectiveness.

Randomised controlled trials (RCTs):

- 8 RCTs[22–29]

Other studies:

- Four uncontrolled trials (UCT)/case series.[30–33]
- One pragmatic outcome study.[34]
- Many single-case reports/studies (over 100).
- A number of surveys and audit/patient outcome studies.
- No relevant qualitative research studies were located.

Studies excluded:

- Benzecri *et al*[35] and Cialdella *et al*[36]—withdrawal or substitution of anxiolytics (benzodiazepines).
- Gottwald and Weisner[37]—nervousness/restlessness with or without fever in infants and children—uncontrolled study with no clear measure of anxiety.
- Oberbaum *et al*[38]—pain and anxiety in orthopaedic patients—uncontrolled study (case series) with no clear measure of anxiety.
- Julian[39]—homeopathic pathogenetic trial ('proving').
- Zenner and Weisner[40]—gynaecological disorders including mood disorders—uncontrolled study with no clear measure of anxiety.
- Hariveau *et al*[41]—school phobia/stress in children—uncontrolled study with no clear measure of anxiety.

The evidence

Eight relevant RCTs were located. The types of anxiety and anxiety disorders studied were test anxiety, generalised anxiety disorder, anxiety related to medical or physical conditions such as cancer or surgical procedures. The studies are presented in the tables with comments on their methodology and clinical relevance (Table 1).

Summary of studies

Test anxiety

Stanton[28] reported a placebo-controlled trial of a homeopathic preparation (Argentum nitricum 12 ×) for test anxiety in 40 subjects in 1981. Test anxiety as measured by the Test Anxiety Scale (TAS) was reported to be significantly reduced with the homeopathic preparation compared with placebo. The original article was unavailable so that it was not possible to rate the quality.

Baker and colleagues[23] attempted a replication of this study. The study was conducted in an Australian University with 70 test anxious student volunteers and the methodology used was rigorous with adequate randomisation to one of three arms, traditional homeopathy, radionic[1] or placebo. Concealment of allocation and blinding of students and assessors were also acceptable and a positive check on power at the end of the study was obtained (62 completed the study) with the study adequately powered to demonstrate a 5% difference between groups. A revised version of the TAS was used, and comparison with Stanton's data suggested that anxiety scores pre-treatment might have been slightly higher in the earlier study but analysis of the data revealed no significant difference between the groups for reduction in test anxiety. Both of the test anxiety studies used the same, single homeopathic medicine, but without the individualised prescribing usually associated with the prescription of single homeopathic medicines. Baker *et al* attempted to determine whether students who fitted the 'Argentum nitricum profile' responded better than those who did not, but their study lacked the power to do this reliably. The nature of the 'Argentum nitricum profile' or how or when it was determined is not described.

Moderate anxiety and generalised anxiety disorder

Two randomised controlled trials have been conducted on adult patients with anxiety, one on 77 adults with above average anxiety scores (mean Spielberger State-Trait Anxiety Inventory [STAI] scores between 40 and 50 for state and trait anxiety) but no specific diagnosis[27] and one on 44 adults diagnosed with generalised anxiety disorder.[24] The studies differed in that the first utilised a proprietary homeopathic complex 'Anti-anxiety' (constituents listed in table of studies) while in the latter study, single homeopathic medicines were prescribed on an individualised basis (classical homeopathy). Both studies appear to incorporate reasonably rigorous methodology including adequate concealment of allocation and blinding although the method of generating the randomisation sequence was not reported in either case.

In the first trial, no significant between group differences were found either at pre- or post-test on STAI but there were differences in sleep loss with those in the homeopathy group reporting significantly less loss of sleep.[27] The author concluded that the homeopathic complex, 'Anti-anxiety' may be useful for this aspect of anxiety although it appeared to have little value in the reduction of either state or trait anxiety.

Bonne and colleagues[24] reported no significant difference between adults with generalised anxiety disorder treated with individualised remedies and those treated with placebo for 10 weeks. In fact, a significant improvement was observed in both the active and placebo groups, including reduction in Hamilton Rating Scale for Anxiety (HAM-A) scores, over the period of the study. However, this study may have been underpowered, as a power calculation had demonstrated that a minimum of 60 participants was required but only 44 were recruited.

Other anxiety disorders

Two randomised controlled trials of proprietary homeopathic complexes appear to address mixed anxiety and depressive disorder rather than an anxiety disorder.[25,26] Neither of the studies incorporated a placebo arm and in both studies, benzodiazepines were used as the comparator (lorazepam and diazepam, respectively). As these agents are primarily anxiolytic, it appears that the anxiety component of the condition was being treated. The homeopathic complex was reported to be as effective as the benzodiazepine but this may be a result of the studies being insufficiently powered to detect a difference. Concerns over the initial diagnosis of participants together with a lack of detail about the methodology and outcome measures limit the usefulness of these findings.

Davidson *et al*[31] reported an uncontrolled study of homeopathic treatment of a series of 12 patients with a range of diagnoses related to depression and anxiety disorders including 10 with social phobia, either as the sole diagnosis or combined with panic disorder, major depression or attention deficit hyperactivity disorder (ADHD). Full psychiatric diagnostic assessment and a comprehensive homeopathic interview was performed, followed by individualised prescribing of the homeopathic treatment. Seven (58%) of patients were reported to have responded to homeopathic treatment, on the basis of the Clinical Global Improvement (CGI)

[1]'Radionic' homeopathy is not a recognised form of homeopathy; homeopathic medicines produced by this method are not recognised as such by any homeopathic pharmacopoeia.

Table 1 Summary of studies

Study	*Study design*	*Sample*	*Inclusion criteria*	*Homeopathy intervention (Tx)*	*Control intervention (Ct)*	*Outcome measure(s)*	*Results*	Methodology comments and Jadad score*	*Clinical comments*
Randomised controlled trials									
Alibeu and Jobert[22] (French)	RCT	50 hospitalised children (6 months–14 years) Selection process unclear Tx = 23 Ct = 24	Post-operative agitation (anxiety)	*Aconite* No. of doses not stated	Placebo (verum)	Not stated except for 'improvement' (physician assessment according to Linde et al[14])	'Effective with 95% good results' Negative outcomes: not mentioned	Randomisation: unknown Allocation concealment: unknown Blinding: unknown Power: not mentioned Attrition rate: unknown Jadad score: 2	On abstract only: Intervention and control appropriate. Outcomes unclear Very high response rate
Baker *et al*[23]	RCT 3-arm	70 of 113 Australian university student volunteers	Test anxiety	Traditionally prepared *Argentum nitricum* 12 ×	1. Radionically prepared *Argentum nitricum* 12 ×	Benson Revised Test Anxiety Scale (RTA)	No significant difference found between treatments on either RTA or TAS	Randomisation: adequate Allocation concealment: adequate Blinding: adequate Power: adequately powered Attrition rate: 8 (11%) Jadad score: 4	Intervention, placebo and outcomes appropriate
		Tx = 21 Ct 1(R) = 18 Ct 2(P) = 23 [completers only]	Score of 50+ on Benson RTA	Twice daily for 4 days	2. Placebo Alcohol/water mixture as per treatments	TAS 36-item *A. nitricum* questionnaire Pre and post (1 week later)	Negative outcomes: not mentioned		High-quality study
Bonne *et al*[24]	RCT	44 selected from 247 adults recruited via adverts	Generalised anxiety disorder (DSM-IV diagnosis)	Individualised homeopathy (single remedy, all dilutions $>10^{-30}$) 10 weeks	Placebo 'Non-medication impregnated globules'	HAM-A HAM-D BSI PGWBI BDI STAI subjective distress (VAS)	Significant improvement in most measures including HAM-A in both groups. No significant difference between groups	Randomisation: unknown Allocation concealment: adequate Blinding adequate Power: calculation suggested target of 60 Attrition rate: 5 (11%) Jadad score: 3	Intervention, control and outcomes appropriate but follow-up short for GAD.
		Tx = 22 Ct = 22	HAM-A > 20 HAM-D < 18			Pre, mid and post	Negative outcomes: no aggravations observed		
Hariveau[25] (French)	RCT 2 centres	84 (no statement on numbers in each group)	Reactive anxiety-depression	Lithium Microsol 3–4 ampoules per day, twice daily 30 days	Lorazepem 2–4 mg per day, twice daily	Measures not stated—sleep, delay in sleep onset, heart rate, 'emotionalism'	Outcomes measured after 30 days, measures used not described Negative outcomes: not mentioned	Randomisation: unknown Allocation concealment: unknown Blinding: unknown Power: no mention Attrition: unknown Jadad score: 1	Not sent for clinical commentary—no English abstract
Heulluy[26]	RCT (non-blinded)	N = 60 setting and recruitment unknown Tx = 30 Ct = 30	'Currently under consultation for depression, postmenopausal involution or thymo-effective dystonia'	Non-individualised L72 (constituents not specified) (20 drops 4 times daily for 31 days) dose increased if required	Diazepam (dose and frequency unknown)	Ratio of pre and post scores for selected items on HAM scale	'L72 as effective as diazepam on all measures' Negative outcomes: drowsiness (1 case for L72, 2 for diazepam)	Randomisation: unknown Allocation concealment: unknown Blinding: open study Power: not mentioned Attrition rate: unknown Jadad score: 1	Intervention appropriate Control unclear Outcomes Inappropriate Diagnostic classification a problem

Table 1. (*continued*)

Study	*Study design*	*Sample*	*Inclusion criteria*	*Homeopathy intervention (Tx)*	*Control intervention (Ct)*	*Outcome measure(s)*	*Results*	Methodology comments and Jadad score*	*Clinical comments*
McCutcheon[27]	RCT	77 recruited via students and health food store	Above average anxiety scores (score of 18+ on part one of pre-test STAI)	Anti-Anxiety,* 15 days	Placebo	STAI	No significant differences in STAI or pulse rate between groups Significantly less sleep loss in homeopathy group	Randomisation: unknown Allocation concealment: adequate Blinding: adequate Power: not reported Attrition rate: 5 (6%)	Intervention, control and outcomes appropriate but sleep disturbance is not a core symptom of anxiety
		Tx = 38 Ct = 39		20 drops 4 times daily		Resting pulse Sleep loss	Negative outcomes: not mentioned	Jadad score: 4	
Stanton[28] (details reported in Baker *et al*[23] original report unavailable)	RCT	40	Test anxiety	*Argentum nitricum* 12 ×	Placebo	Test Anxiety Scale	Homeopathic preparation significantly improved test anxiety compared with placebo	No details available Jadad score:?	Not sent for clinical commentary
Thompson *et al*[29]	RCT	53	Symptoms of oestrogen withdrawal (including anxiety)	Individualised prescribing (60 minute initial consultation plus four 20 minute follow-up consultations	Matched placebo tablet, granule or liquid	Primary: MYMOP	No difference between groups for either activity or profile scores.	Randomisation: adequate Allocation concealment: adequate Blinding: adequate Power: post hoc calculations	Large number (71) of homeopathic medicines used, intensive follow-up
				Duration 16 weeks		Secondary: HADS Menopausal Symptom Questionnaire EORTCQLQ-C30	Clinically relevant improvements in symptoms and mood for both groups. Negative outcomes: approx 25% in each group	suggested 65–175 per group required Attrition rate: 5 from homeopathy group, 3 from placebo, reasons documented Jadad score: 5	Outcomes clinically significant in both groups Adverse events appear more common than in other trials. No details of nature of adverse events given
Uncontrolled studies (anxiety disorders)									
Davidson *et al*[31]	UC study	12 patients at US hospital or homeopathic hospital. Recruitment process unclear	Social phobia, panic disorder, residual attention-deficit hyperactivity disorder, major depression, chronic fatigue syndrome	Full psychiatric assessment and homeopathic interview then individualised prescribing	N/A	CGI plus self-rated SCL-90 in the hospital, BSPS in the medical practice.	58% (7) recorded a 50% reduction on the CGI scale	Not randomised, controlled or blinded.	Intervention and outcomes appropriate
						Measures taken at variable intervals	50% (6) recorded a 50% reduction on the SCL-90 or BSPS scale	Compliance unknown	Control/placebo N/A
				Duration variable: 7–80 weeks			Negative outcomes: none reported	Co-interventions—partial (drug and dose reported not frequency)	Very relevant, excellent preliminary report
Uncontrolled studies (anxiety in physical or medical conditions)									
Clover *et al*[30]	Case series	50 cancer patients referred to UK homeopathic hospital	Cancer-related symptoms (including anxiety)	Individualised homeopathy	None	HADS Rotterdam Symptom Checklist (RSCL)	Improvements on the psychological distress subscale of RSCL	Not randomised or blinded	Intervention,outcomes appropriate (latter for quality of life)

	Consecutive patients					Initial, 2nd, 3rd and 4th clinic attendances	Initial visit 48% patients with normal HADS anxiety scores, 75% at 4th visit.	Attrition rate: 58% at 6 months (15 died, 14 withdrew for various reasons ,0 lost to follow-up) Co-interventions: 29 (58%) prescribed iscador, 50% relaxation, 14% acupuncture, 34% CAM elsewhere	Control/placebo N/A Well-designed pragmatic cohort study
Thompson and Reilly[32]	UC study/case series (consecutive patients)	100 cancer patients referred to UK homeopathic hospital cancer clinic	Cancer-related symptoms (including anxiety)	Sixty minute consultation and prescription of individualised remedy Duration—variable	N/A	Self-rating of symptoms on 11-point scale HADS EORTC QLQ-30 At initial and 4–6 consultations later	Initially 59 with anxiety, 37 with depression. Mean anxiety scores improved by 1.6 (95%CI 0.4–2.9), mean depression scores by 1.4 (0.1–2.6) 17 patients with aggravation/return of old symptoms	Not randomised or blinded Attrition rate: 44% 56 completed (26 died, 18 defaulted) Cointerventions and other confounders: unknown	Intervention and outcomes appropriate Control/placebo N/A Excellent case series/ cohort study
Thompson and Reilly[33]	UC study/case series (consecutive patients)	45 breast cancer patients (26 from previous study) referred to UK homeopathic hospital	Symptoms of oestrogen withdrawal (including anxiety)	60 minute consultation and Rx of individualised remedies for up to 3 symptoms Duration—variable	N/A	Score of an effect on daily living of 3 symptoms (unvalidated) Symptom scores HADS EORTC QLQ-30	Significant improvement in all 3 main symptoms Mean anxiety scores improved by 2.1 (95%CI 0.7–3.4) Negative: 7 patients with new symptoms, 10 return of old symptoms. 1 patient withdrew due to symptoms	Not randomised or blinded Attrition rate: 11% 40 completed (1 died, 4 defaulted) Cointerventions: reported	Intervention and outcomes appropriate Control/placebo N/A Good study design but see Thompson and Reilly[35]

Jadad score: Point for each of following—described as randomised, randomisation appropriate, described as double-blinded, double blinding appropriate, description of withdrawals and dropouts (maximum 5 points).[52]

*Anti-anxiety constituents: *Cicuta virosa, Ignatia, Gaultheria, Asafoetida, Corydalis, Sumbulis, Valeriana officinalis, Hyoscyamus, Avena sativa.*

scale including two of the patients with social phobia, two cases of social phobia combined with panic disorder and one with social phobia combined with major depression. Classical homeopathy was used and, as is typical of this form of homeopathy, a range of different medicines and dilutions were used. Duration of treatment and co-interventions varied between patients, as did the initial diagnoses, leading to difficulties in interpreting the results. However, this study is relevant to practice and is a useful preliminary report.

Anxiety associated with medical or physical conditions

A randomised controlled trial of a single homeopathic medicine (*Aconite*) for post-operative agitation in children suggested that this might be an appropriate treatment as '95% good results' were reported.[22] However, no clear objective outcome measures are provided and many of the methodological details, such as randomisation, allocation concealment and blinding are unclear.

Thompson and colleagues[29] recently reported a rigorously conducted randomised placebo-controlled trial of homeopathy for the treatment of oestrogen withdrawal in 53 breast cancer patients. The authors report that both groups showed clinically important improvements based on Measure Yourself Medical Outcome Profile (MYMOP) scores over the 16 week trial period. However, the study failed to show that the specific effect of the remedy added further to the non-specific effects of the consultation, possibly due to lack of power. Mean Hospital Anxiety and Depression Scale (HADS) anxiety scores in the active and placebo groups indicated mild anxiety initially (9.2 in the active group and 8.7 in the placebo group). These scores reduced to 8.1 and 7.4 respectively but no significant difference was found between the two groups at the end of the study.

Other studies of homeopathy for anxiety in cancer patients are all uncontrolled and involve the use of homeopathy to treat a range of problems with anxiety constituting only one of the reported outcomes. The lack of a control group and reporting of a range of outcomes leads to difficulties in interpretation of the results, particularly when assessing the extent to which any response is due solely to treatment with homeopathy. Nevertheless, the findings are relevant to practice and therefore will be described here.

Clover and colleagues[30] reported an uncontrolled study of 50 cancer patients in whom response to homeopathy treatment was assessed using the HADS and Rotterdam Symptom Checklist. Improvements were seen on the HADS Anxiety subscale when comparing scores on initial and later (3rd) visits and the percentage with normal HADS anxiety scores increased from 48% to 75% by the 4th visit. However, the lack a control group, variable co-interventions and loss to follow-up of 58% lead to difficulties in interpretation of these findings.

In a well-designed uncontrolled study of individualised homeopathy for symptom relief in 100 cancer patients, 63% of patients completing the study were found to have some improvement in anxiety scores at the end of the study period.[33] Up to three symptoms perceived by the patient as problematic were rated on a self-rating scale while anxiety was assessed using the Hospital Anxiety and Depression Scale (HADS). At the beginning of the study, 59 patients were found to be anxious with 30 having anxiety (scores above 10), 29 borderline anxiety (scores 8–10), and a greater percentage of those with metastatic disease being anxious (67% compared with 52%). The mean overall improvement in anxiety scores was 1.6 (95% CI 0.4–2.9) but the attrition rate was high. Seventeen patients suffered an aggravation of symptoms or return of old symptoms considered to be previously described remedy reactions but no adverse reactions resulted in withdrawal of treatment. Satisfaction with treatment was measured by self-completion questionnaire and was high amongst those who completed the study; 75% regarded homeopathic treatment as having been helpful or better.

In a further uncontrolled study by the same authors, individualised homeopathy was used to treat symptoms of oestrogen withdrawal in 45 breast cancer patients. A significant improvement in anxiety scores was reported with mean change being 2.1 (95% CI 0.7–3.4).[32] Twenty six of the patients had also been included in the 2002 study. Eighty nine per cent of patients completed this study and again satisfaction with treatment was high; 67% regarded homeopathic treatment as having been helpful, very helpful or extremely helpful for their symptoms.

Pragmatic and outcome studies

A large-scale pragmatic study comparing the outcomes was reported two types of care for patients with anxiety disorders conducted in France, compared the efficacy, utility and costs of two strategies: homeopathic general practitioners with 'homeopathic orientation' *vs* general practitioners without 'homeopathic orientation'.[34] Outcomes of 394 patients were studied and the findings revealed that the effectiveness of the two strategies, based on improvement in HAM-A and STAI scores, was equivalent. Utility/satisfaction was also equivalent but the costs associated with care by a homeopathic general practitioner were greater. These increased costs were particularly associated with increased cost of medication and consultations. Medication costs were caused by greater number of products prescribed by the homeopathic practitioners, and the fact that a greater proportion of these products were non-reimbursable. Overall, the increased costs were mainly borne by the patient rather than the social security system.

Finally, outcome studies or audits such as those of Clover[42] and Richardson[43] have reported positive

results in patients with a range of conditions including anxiety while van Wassenhoven and Ives[19] have reported positive outcomes on psychological symptoms in general. As with other uncontrolled studies, any response or improvement in the condition may be due to a number of factors and cannot be assigned to homeopathy alone.

Discussion

It is difficult to interpret the evidence on the benefit of homeopathy in anxiety and anxiety disorders because of heterogeneity of diagnoses and patient groups, type of homeopathy, and weaknesses of methodology and reporting. Studies have been conducted using a range of methodologies in a number of different conditions. While several uncontrolled and observational studies have demonstrated positive results including high levels of patient satisfaction, because of the lack of a control group, it is difficult to assess the extent to which any response is due to homeopathic treatment. The interventions varied and included standard complexes, classical and clinical homeopathy. For practical reasons when individualised (classical and clinical) homeopathy was used, prescribing was sometimes restricted to limited lists of medicines, further complicating interpretation and application to other settings and patient groups.

A number of randomised controlled trials have been conducted. The study conducted by Baker *et al*[23] on test anxiety used rigorous methodology but contradicted the findings of an earlier study, which it had attempted to replicate. The studies by McCutcheon[27] on patients with moderate anxiety scores and Bonne *et al*[24] also incorporated reasonably rigorous methodology. In neither case was homeopathic treatment shown to be more effective than placebo but these studies were of small scale and may have been underpowered. Although Bonne and colleagues[24] reported no significant difference between adults with generalised anxiety disorder treated with individualised remedies and those treated with placebo for 10 weeks, a significant improvement was observed in both the active and placebo groups, including reduction in Hamilton Anxiety Scale scores, over the period of the study. This raises the issue of the placebo and Hawthorne effect and their clinical importance in such conditions. Of the controlled trials, only that by Bonne *et al* utilised individualised prescribing while the other studies involved use of a standard or proprietary remedy.

Vainchtock *et al*'s[34] observational study was of pragmatic design, comparing the outcomes of patients cared for by allopathic and homeopathic general practitioners. On the basis of clinical and utility outcomes it would appear that the two strategies are equivalent which suggests that homeopathy-led care for those with anxiety disorders may be worthy of consideration. One note of caution is that all those providing care were physicians and occasionally utilised interventions other than homeopathic remedies. Additionally, the costs to the patient were greater for homeopathy-led care compared with allopathic care, although this is likely to be specific to the French health care system.

The variation in condition, methodology and intervention prevent formal statistical synthesis of the research findings and a meta-analysis would not be appropriate. However, the included studies are presented in the tables together with comments on their methodology and clinical relevance in an attempt to highlight the issues to be addressed in future research in this area. A substantial number of case studies were located and consideration of a strategy to utilise these as a potential form of evidence may be valuable. These studies also provide an illustration of the ways in which homeopathy is utilised in individuals with anxiety.

Adverse effects reported in the studies located appear limited mainly to 'remedy reactions' or 'aggravations' including temporary worsening of symptoms, and reappearance of old symptoms. These reactions were generally transient but in one study, aggravation of symptoms caused withdrawal of the treatment in one patient. The literature on the safety of homeopathy suggests that homeopathic medicines may provoke adverse effects but these are relatively rare, mild and transient, although there is probably underreporting.[44,45] The situation with regard to safety can be summed up as follows:

> 'Homeopathic medications in high dilutions prescribed by trained professionals are probably safe and unlikely to provoke severe adverse reactions. It is difficult to draw definite conclusions due to the low methodological quality of reports claiming possible adverse effects of homeopathic medicines'.[44]

Conclusions

A comprehensive search demonstrates that the evidence on the benefit of homeopathy in anxiety and anxiety disorders is limited. A number of studies of homeopathy in such conditions were located but the randomised controlled trials report contradictory results, are underpowered or provide insufficient details of methodology. Several uncontrolled and observational studies reported positive results including high levels of patient satisfaction but because of the lack of a control group, it is difficult to assess the extent to which any response is due to homeopathy. Adverse effects reported appear limited to 'remedy reactions' and included temporary worsening of symptoms and reappearance of old symptoms. On the basis of this review it is not possible to draw firm conclusions on the efficacy or effectiveness of homeopathy for anxiety.

Implications for the future

Homeopathy appears to have a number of potential advantages: high acceptability to patients, as reflected in the high proportion of patients suffering from anxiety who spontaneously seek homeopathic treatment, a consistent finding from surveys in several countries; safety and absence of dependency; and possibly relatively low cost. The low cost of the medicines may, however be offset by longer or more frequent consultations and costs may vary between countries and systems of reimbursement.

Further research is required and should incorporate (or be preceded by) qualitative investigation, aimed at understanding why patients with anxiety disorders seek homeopathic treatment, their perception of and satisfaction with the process and the benefits they perceive or hope to achieve. We were unable to identify any studies of these questions focussing on anxiety, although a study of patients attending an NHS centre indicated that its perceived safety is an important motivating factor for patients seeking homeopathic treatment for a range of conditions, including psychological problems.[46]

Studies should be well-designed, with sufficient numbers of participants and clearly defined inclusion criteria. Outcome measures should be appropriate and measure the benefits which are important to patients.

Anxiety disorders are common and treatment in primary care settings is the preferred approach,[47] it is therefore important that research is valid for this setting. Low recruitment ratios are typical of randomised controlled trials in the primary care setting[48,49]; this appears to be particularly the case for psychological problems[50] and has been encountered in primary care-based RCTs of homeopathic treatment of psychological problems.[51] Although, in principle, this problem could be overcome by using a very large recruitment base, and accepting low recruitment ratios, the recruited sample is unlikely to be typical of the population. Additionally, such studies are likely to be expensive and cumbersome. The reasons for the recruitment problems are not fully understood, but appear to include patient preference issues (including aversion to blinding), and reluctance to recruit on the part of primary care providers.

An important objective of qualitative research is to discover research designs which are acceptable to patients and their health care providers, and thus associated with improved recruitment ratios. There are a number of problems with currently available treatments for anxiety, these include patient choice/preference issues and compliance (the two issues are linked), dependency (particularly with benzodiazepines) and adverse effects. These problems are generally not best investigated by classical double-blind, placebo-controlled RCT designs. Possible solutions to these problems and the recruitment difficulties include cohort studies and the use of preference arms, or pragmatic studies in which patients receive individualised homeopathic treatment and this is compared to conventional care. While these methods sacrifice some rigour in terms of determining narrow efficacy, with good design, this will be more than compensated by the gain in terms of improved recruitment ratios, incorporation of patient preference, compliance and dependency; these are prominent issues in the 'real world' treatment of anxiety, especially in primary care.

The availability of adequately trained and accredited homeopathic practitioners is another significant constraint to clinical trials of homeopathy for anxiety. Possible solutions include the use of homeopathic complexes, questionnaire-driven prescribing and limited training of existing health professionals, but all of these would require validation.

Acknowledgements

Anelia Boshnakova, Electronic Information Officer, RCCM for advice and support with search strategies and searches. Annette Gamblin, Senior Lecturer, School of Integrated Health, University of Westminster for interpretation of non-English language studies. Hugh McGuire, Trials Search Co-ordinator, Cochrane Depression, Anxiety & Neurosis Group for translation and appraisal of several studies. The Project Advisory Group and Specialist Advisory Group (mental health) for the NHS Priorities Project for advice and support to the project.

The NHS Priorities Project is funded by the Department of Health. The views and opinions expressed are those of the authors and do not necessarily reflect those of the Department of Health.

References

1 Churchill R, Barbui C, Furukawa T, *et al.* Depression, anxiety and neurosis group (Collaborative Review Groups). *About the Cochrane Collaboration*. Cochrane Library 2005, Issue 4.

2 Jenkins R. *Introduction to Generalised Anxiety*. WHO UK Collaborating Centre, 2005. Available at National Library for Health, Mental Health Specialist Library: http://libraries.nelh.nhs.uk/mentalhealth. Accessed March 2006.

3 Office for National Statistics. *Psychiatric Morbidity among Adults living in Private Households, 2000: Summary Report*. London: HMSO, 2000.

4 Eisenberg DM, Davis RB, Ettner SL, *et al.* Trends in alternative medicine use in the United States, 1990 1997: results of a follow-up national survey. *JAMA* 1998; **280**: 1569–1575.

5 Unutzer J, Klap R, Sturm R, *et al.* Mental disorders and the use of the alternative medicine: results from a national survey. *Am J Psychiatry* 2000; **157**(11): 1851–1857.

6 Davidson J, Rampes H, Eisen M, *et al.* Psychiatric disorders in primary care patients receiving complementary medical treatments. *Compr Psychiatry* 1998; **39**: 16–20.

7 Trichard M, Lamure E, Chaufferin G. Study of the practice of homeopathic general practitioners in France. *Homeopathy* 2003; **92**: 135–139.

8 Long L, Huntley A, Ernst E. Which complementary and alternative therapies benefit which conditions? A survey of the opinions of 223 professional organizations. *Complement Ther Med* 2001; **9**: 178–185.
9 Lockie A. *Homeopathy Handbook*. London: Dorling Kindersley, 2001.
10 Peters D editor. *New Medicine*. London: Dorling Kindersley, 2005.
11 Thomas K, Nicholl J, Coleman P. Use and expenditure on complementary medicine in England: a population based survey. *Complement Ther Med* 2001; **9**: 2–11.
12 Alternative Healthcare. *Market Assessment*. London: Key Note, 2001.
13 Kleijnen J, Knipschild P, ter Riet G. Clinical trials of homeopathy. *BMJ* 1991; **302**: 316–323.
14 Linde K, Clausius N, Ramirez G, *et al.* Are the clinical effects of homoeopathy placebo effects? A meta-analysis of placebo-controlled trials. *Lancet* 1997; **350**: 834–843.
15 Cucherat M, Haugh MC, Gooch M, Boissel JP. Evidence of clinical efficacy of homeopathy: a meta-analysis of clinical trials. *Eur J Clin Pharmacol* 2000; **56**: 27–33.
16 Shang A, Huwiler-Müntener K, Nartey L, *et al.* Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. *Lancet* 2005; **366**: 726–732.
17 Knaudt P, Connor K, Weisler R, Churchill L, Davidson J. Alternative therapy use by psychiatric outpatients. *J Nerv Ment Dis* 1999; **187**: 692–695.
18 Demling J, Neubauer S, Luderer HJ, Worthmuller M. A survey on psychiatric patients' use of non-medical alternative practitioners: incidence, methods, estimation, and satisfaction. *Complement Ther Med* 2002; **10**(4): 193–201.
19 Van Wassenhoven M, Ives G. An observational study of patients receiving homeopathic treatment. *Homeopathy* 2004; **93**: 3–11.
20 CRD (NHS Centre for Reviews and Dissemination) Report Number 4 (2nd edn), *Undertaking Systematic Reviews of Research on Effectiveness*. York: CRD, 2001.
21 Jorm AF, Christensen H, Griffiths KM, Parslow RA, Rodgers B, Blewitt KA. Effectiveness of complementary and self-help treatments for anxiety disorders. *Med J Aust* 2004; **181**: S29–S46.
22 Alibeu JP, Jobert J. [Aconite in homeopathic relief of post-operative pain and agitation in children.] Aconit en dilution homeopathique et agitation post-operatoire de l'enfant. *Pediatrie* 1990; **45**: 465–466 (Also reported as Alibeu J, Jobert J. Etude sur Aconit en dilution homeopathique sur l'agitation post-operatoire de l'enfant. *Homeopathie Francaise* 1992; **80**:10–12.).
23 Baker DG, Myers SP, Howden I, Brooks L. The effects of homeopathic *Argentum nitricum* on test anxiety. *Complement Ther Med* 2003; **11**: 65–71.
24 Bonne O, Shemer Y, Gorali Y, Katz M, Shalev A. A randomized, double-blind, placebo-controlled study of classical homeopathy in generalized anxiety disorder. *J Clin Psychiatry* 2003; **64**: 282–287.
25 Hariveau E, Albertini C, Rufo M. Comparaison de Lithium Microsol a lorazepam dans les manifestations anxiodepressives reactionnelles de l'adulte [Comparison of Lithium Microsol with lorazepam in reactive anxiodepressive manifestation in adults.]. *Homeopathie Francaise* 1991; **79**: 59–62.
26 Heulluy B. Essai randomisé ouvert de L 72 (spécialité homéopathique) contre diazépam 2 dans les états anxiodépressifs [Randomised trial of L.72 (homeopathic speciality) with Diazepam 2 in cases of nervous depression.] Laboratoires Lehning, Metz; Unpublished study, 1985.
27 McCutcheon L. Treatment of anxiety with a homeopathic remedy. *J Appl Nutr* 1996; **48**: 2–6.
28 Stanton HE. Test anxiety—a five drop solution. *Educ News* 1981; **17**: 12–15.
29 Thompson EA, Montgomery A, Douglas D, Reilly D. A pilot, randomized, double-blinded, placebo-controlled trial of individualized homeopathy for symptoms of estrogen withdrawal in breast-cancer survivors. *J Altern Complement Med* 2005; **11**: 13–20.
30 Clover A, Last P, Fisher P, Wright S, Boyle H. Complementary cancer therapy: a pilot study of patients, therapies and quality of life. *Complement Ther Med* 1995; **3**: 129–133.
31 Davidson JRT, Morrison RM, Shore J, Davison RT, Bedayn G. Homeopathic treatment of depression and anxiety. *Altern Ther Health Med* 1997; **3**: 46–49.
32 Thompson EA, Reilly D. The homeopathic approach to symptom control in the cancer patient: a prospective observational study. *Palliat Med* 2002; **16**: 227–233.
33 Thompson EA, Reilly D. The homeopathic approach to the treatment of symptoms of oestrogen withdrawal in breast cancer patients. A prospective observational study. *Homeopathy* 2003; **92**: 131–134.
34 Vainchtock A, Dansette GY, Nicoloyannis N, *et al.* Medicoeconomic evaluation of management of anxiety disorders in outpatient care. *Health and System Science* 2000; **4**: 103–155.
35 Benzecri JP, Maiti GD, Belon P, Questel R. Comparaison entre quatre méthodes de sevrage après une thérapeutique anxiolytique. [Comparison of four methods of withdrawal from anxiolytic therapy.]. *Les Cahiers de l'Analyse des Données* 1991; **16**: 389–402.
36 Cialdella P, Boissel JP, Belon P. Specialites homeopathiques en substitution de benzodiazepines: etude en double-insu vs. placebo [Homeopathic specialties as substitutes for benzodiazepines: double-blind vs. placebo study.]. *Therapie* 2001; **56**: 397–402.
37 Gottwald R, Weiser M. Antihomotoxische Behandlung von Unruhezustanden mit und ohne Fieber bei Kindern: Ergebnisse einer Anwendungsbeobachtung. *Biol Medizin* 1999; **28**: 308–312.
38 Oberbaum M, Schreiber R, Rosenthal C, Itzchaki M. Homeopathic treatment in emergency medicine: a case series. *Homeopathy* 2003; **92**: 44–47.
39 Julian OA. A comparative psychosomatic and pharmacological study, in man and animal, within homeopathic medicine. *Annales de Therapeutique Psychiatrique* 1967; **3**: 305–309.
40 Zenner S, Weiser M. Homeopathic treatment of gynecological disorders: results of a prospective study. *Biomed Ther* 1999; **17**: 31–35.
41 Hariveau E, Rufo M, Albertini C. Lithium Microsol dans le stress de l'ecolier. [Lithium microsol in school stress]. *Homeopathie Francaise* 1991; **79**: 56–58.
42 Clover A. Patient benefit survey: Tunbridge Wells Homoeopathic Hospital. *Br Homeopath J* 2000; **89**: 68–72.
43 Richardson WR. Patient benefit survey: Liverpool Regional Department of Homoeopathic Medicine. *Br Homeopath J* 2001; **90**: 158–162.
44 Dantas F, Rampes H. Do homeopathic medicines provoke adverse effects? A systematic review. *Br Homeopath J* 2000; **89**: S35–S38 [Full text available at http://www.rlhh.org.uk/conference/ (Proceedings 2)].
45 Fisher P, Dantas F, Rampes H. The safety of homeopathic products. *J R Soc Med* 2002; **95**: 474–475.
46 Sharples F, Van Haselen R, Fisher P. NHS patients' perspective on complementary medicine. *Complement Ther Med* 2003; **11**: 243–248.
47 McIntosh A, Cohen A, Turnbull N, *et al. Clinical Guidelines and Evidence Review for Panic Disorder and Generalised Anxiety Disorder*. Sheffield: University of Sheffield/London, National Collaborating Centre for Primary Care, 2004.

48 Wilson S, Delaney C, Roalfe A, *et al.* Randomised trials in primary care: case study. *BMJ* 2000; **321**: 24–27.

49 Bell-Syer S, Moffett J. Recruiting patients to randomised trials in primary care: principles and case study. *Fam Pract* 2000; **17**: 187–191.

50 Hunt C, Shepherd L, Andrews G. Do doctors know best? Comments on a failed trial. *Med J Aust* 2001; **174**: 144–146.

51 Katz T, Fisher P, Katz A, Davidson J, Feder G. The feasibility of a randomised, placebo controlled clinical trial of homeopathic treatment of depression in general practice. *Homeopathy* 2005; **94**: 145–152.

52 Jadad AR, Moore RA, Carroll D, *et al.* Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996; **17**: 1–12.