



Prim Care Clin Office Pract
29 (2002) 407–418

PRIMARY
CARE

Homeopathy

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Why should a physician know about homeopathy?

Homeopathy is used widely. In 1997, it was estimated that nearly 2.5 million patients in the United States alone use complementary alternative medicine (CAM) modalities. In European countries, the number of CAM users is much higher and growing rapidly. Currently, one to two out of three patients use CAM, and approximately 3.4% of those patients use homeopathy [1]. Some physicians use homeopathic remedies for defined disease entities or adopt the use of homeopathic treatment principles for the treatment of several conditions (i.e., acute pain [2], coryza [3], diarrhea [4], hay fever [5], asthma [6], and migraine [7]).

In Europe, homeopathy treatments represent a substantial portion of the over-the-counter market. Indeed, European physicians seem more amenable to homeopathy. More than 10,000 German and French physicians practice homeopathy [8]. On average, 30% of referrals made to the homeopathic hospitals within the United Kingdom come directly from oncologists [9]. A survey of 293 general practitioners in the Netherlands showed that 45% believe that homeopathy is efficacious [10]. Worldwide, \$1 billion per year is spent on homeopathic medications [11]. The effects of homeopathy can be long lasting; 1 year after seeing a homeopath, nearly 75% of patients report marked or moderate improvements [12].

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History and philosophy

Homeopathy dates back 2400 years ago to Hippocrates [13]. Modern homeopathy dates back to the 1800s, when Samuel Hahnemann, a German physician, conducted a self-experiment with cinchona, a bark used as a remedy for fever. He found that when a healthy person took large doses of cinchona, he or she would experience exactly the symptom that this plant was thought to correct, in this case, fever. From this, Hahnemann developed the theory of *Similia Similibus Curantur*-like cures like, or the law of similars [14], which is an extension of Hippocrates' observations. Hahnemann theorized that small doses of cinchona would be of benefit in fighting fever and consequently, he arrived at the principle of dilution, or infinitesimal dose [41].

Hahnemann further observed that in addition to acting on acute conditions, certain remedies exerted their effects based on the constitution of individuals, such as their moral and intellectual character, their habits, their relationships, their likes and dislikes, and what made them feel better or worse. Even the time of day a person's symptoms appear and on what side of the body the ailment appears are taken into consideration. Remedies may have different effects on different individuals, and associations between medications and personality types have been recognized [14,15], from which arose the third principle of homeopathy, individual specificity. In homeopathy, the symptom picture does not equate to disease; rather, it is an adaptation of the body to the stress caused by the disease. Homeopathic treatment acts to shift the body's energy back toward homeostatic balance.

Principles of homeopathy

One guiding principle of homeopathy is the Law of Similars, which posits that a substance that produces symptoms in a healthy person will cure those same symptoms in an ailing person. Also, it is necessary to consider the totality of symptoms in prescribing a homeopathic treatment. One set of symptoms affects the entire body; organs do not respond individually. Physical, emotional, and mental patterns must be matched to the remedy.

Potentization, or the law of the infinitesimal solutions, has probably been the most controversial principle of homeopathy. Potentization is a combination of ultradilution of the substance (dilution of the actual substance to below Avogadro's number of particles) and succussion (vigorous shaking of the substance). Hahnemann implemented succussion when he found that the remedies that were jostled on the way to the home of the patient were more effective than those given in the office without the shaking. He began succussing all remedies before dosing and found an increase in therapeutic effectiveness. The dilution and succussion process allows the energy of the substance to remain, even when present in infinitesimal amounts. In contrast to homeopathy, naturopathy and phytotherapy use herbs in a more allo-

pathic paradigm; they do not follow homeopathic principles (allopathy is derived from the Greek words *allos* (other) plus *pathos* (disease); it is used to differentiate conventional medicine from homeopathy [16]). In modern homeopathy, substances generally are diluted in C (centesimal or 1:100), or X (decimal or 1:10) potencies.

The different homeopathic substances are discovered through provings. In a proving, a well person administers a dose of the remedy to him- or herself and meticulously records the effects that it produces. These findings have been collected into a *Materia Medica*, which categorizes the provings according to body area (for example, Kent's *Repertory of the Homeopathic Materia Medica*, written between 1881–1908) [17].

If the correct remedy is found, an initial worsening of symptoms may occur. If the remedy is not strong enough to provoke an aggravation of the symptoms, it is likely too weak to bring about a cure. In fact, in a recent randomized, controlled trial, it was found that the patients who reported an initial aggravation were those who had the best-sustained outcome [18].

The two different basic types of homeopathic prescribing are acute, which treats a single symptom or condition, and is short-acting; and constitutional, which treats the patient (in toto) and considers mental, emotional, and physical manifestations of the condition to bring about long-term changes in the individual.

Overlap between allopathically accepted principles and the Law of Similars

Several observations in biomedicine are compatible with the Law of Similars:

1. Drugs may induce symptoms that they can relieve. For instance, phenytoin, the widely used antiepileptic medication, may induce seizures at high doses.
2. Drugs may have effects that are opposite to their expected therapeutic activities in some patients; for example, sedatives may lead to agitation in some geriatric patients.
3. Pre-exposure to a low dose of a substance may modulate the response to subsequent exposures, such as desensitization procedures.
4. Biologic agents and drugs can exhibit a nonlinear pharmacodynamic behavior; for example, dobutamine can be a vasodilator at low doses but a vasoconstrictor at high doses [19].

In conventional medicine, if a treatment is proven to work, then knowledge of its mechanism is not required. Examples from conventional medicine can be cited in which the mechanisms are not understood [10].

Until the late 1980s, much of the evidence for homeopathic medicine was anecdotal and in homeopathy textbooks, descriptions of cures were based on the experience of experts. Below is a treatment prescription for the common cold:

When once established and localized, the cure of a Cold is not an easy matter; but a good deal may be done to relieve its symptoms and to shorten its duration. In the “Running Cold” or Fluent Coryza, Mercurius, in medium potencies, is the established remedy, and Bahr advises its use unless the discharge is such as to call for Arsenicum; but I have myself a special favour for Euphrasia, with which I have arrested many a Catarrh of this kind. Arsenicum and Kali bichromicum and Iodatum are also thoroughly Homoeopathic, and are sometimes preferentially indicated: the first when there is prostration like that of Influenza, and the flux is copious, thin and acrid; the second when a foul tongue indicates the involvement of the digestive mucous membrane, the third when the nose is red and swollen externally, the discharge being cool and unirritating. For the “Stuffy Cold” I think that Nux vomica is the specific [14].

In the 1980s, allopathic scientists, often in collaboration with homeopathic prescribers, began to establish randomized, clinical trials that could corroborate or refute claims of efficacy by homeopathic practitioners.

The use of single versus combination remedies is a highly debated topic among homeopaths. Although Hahnemann advocated using a single remedy, modern practitioners have success when using multiple remedies to treat a single condition. The ability to interpret a study that uses combination remedies is a problem inherent in many alternative paradigms.

Mechanism of action

According to the Avogadro law, once a solution of a tincture is diluted beyond 10^{-23} , that solution most likely does not contain a single molecule of active substance. How can such a solution have therapeutic effects?

In the 1990s, physical chemistry theories as to the mechanism of action were postulated. It was found that water forms clathrates, bonds between water molecules surrounding other molecules, which exist even if their core molecules are removed. Because clathrates may behave like crystals, they may replicate themselves during the homeopathic dilution process. The succussion required for the remedy may be similar to the oscillatory nature of crystal growth. Homeopathic medicines in general can be inactivated at 70–80°C, which implies the existence of the microcrystal structure formed by hydrogen bonds [20]. This concept has spurred the theory of water memory effect.

Another mechanism of action uses the logic of recurrent feedback loops. An example of this principle is two tuning forks (for instance A and B) in close proximity. Once tuning fork A is activated, its vibration makes tuning fork B vibrate. Simultaneously, the vibrations from tuning fork B reach back to tuning fork A and established a closed feedback, or recurrent feedback loop. The principle of recurrent feedback loops apply to all dynamic network systems and inexorably lead to the systemic memory hypothesis, which elucidates that complex patterns of emergent information and energy are stored, to various degrees, in physical, chemical, and biologic systems. The addition of resonance, which is a dynamic pattern-recognition process,

explains many classic observations using high-dilution therapies. The systemic memory resonance hypothesis potentially provides a plausible biophysical mechanism not only for explaining how high-dilution therapies contribute to healing, but by extension how information and energy in low-dilution and chemical therapies contribute to healing as well [21]. Nuclear magnetic resonance studies have shown that the addition of a small quantity of a drug followed by successive dilution and mechanical agitation could bring about a significant change in the solution structure [22].

Evaluating the evidence

Animal studies

There are several studies that have used homeopathy effectively in animal populations. An evaluation of Traumeel S (a topical homeopathic preparation) on an animal model of traumatic inflammation showed a decrease in paw edema, associated with the process of healing, was more rapid in rats treated with Traumeel S ($P < 0.05$ at 3 hours; $P < 0.01$ at 5 hours). This finding was associated with a significant decrease in systemic interleukin-6 production, adding further evidence for its anti-inflammatory properties [23].

In a second study, mice were injected with arsenic trioxide, leading to tissue damage. Homeopathic Arsenicum album-30C, or dilute alcohol, was given orally after the injection. The mice fed the homeopathic preparation showed evidence of tissue recovery in terms of enzymatic and histologic changes when compared with control mice. The homeopathic drug was capable of preventing or repairing liver damage induced by arsenic trioxide, and the positive changes were confirmed by the activities of the enzymatic markers [24].

In another study conducted with subject mice, treatment with *Nux vomica* reduced alcohol-induced sleep time from 180 to 270 minutes to less than 150 minutes. The higher the potency administered, the shorter the sleep time relative to the corresponding control. In ultralow concentrations of 1000C, mice woke up after 90 minutes [22].

Human clinical trials

Atopic inhalant allergies

In 51 patients with atopic inhalant allergies, an oral 30C homeopathic preparation (a dose of one drop of substance in 99 drops of water and succussed, repeated 30 times) of their particular allergen or placebo was given. The results revealed a clear objective difference between the effects of placebo and homeopathic remedy on nasal airflow, averaging a 21% improvement from baseline in the treatment group compared with 2% in the placebo group ($P = 0.0001$). Initial aggravations of rhinitis symptoms were provoked more by homeopathy than placebo; by 48 hours after the dose, 29% of the treatment subjects reported worsening, compared with 7% of the placebo group ($P = 0.04$). The patients who had aggravations of symptoms

ultimately had the best outcomes. Compared with placebo, homeopathy provoked a clear, significant, and clinically relevant improvement in nasal inspiratory peak flow, similar to that found with topical steroids [18].

In a small 1994 study by the same investigators, 24 patients with inhalant allergies received either a homeopathic preparation or placebo. Within 1 week, a visual analog scale (a subjective scale in which the subject marks on a standardized line the point at which he or she belongs on the continuum) improved in 5 of 13 placebo cases and 9 of 11 treatment cases. The difference between the groups averaged 33% during the 4-week trial ($P=0.003$). Respiratory function tests showed a change of 10.2% FVC (forced vital capacity) ($P=0.03$) and 14.9% FEV1 (forced expiratory volume in 1 second) ($P=0.08$) in subjects using homeopathy. The homeopathy group showed a trend toward greater reduction in bronchial reactivity with a median increase of 53% in histamine resistance, compared with a median decrease of 7% in the placebo group. Meta-analysis of the three trials indicated a mean advantage of homeopathy over placebo. On average, improvement with homeopathic remedies appears by the second week and results in 33% fewer symptoms. The placebo group showed only 10% fewer symptoms in weeks 3 and 4 [25].

In another randomized, placebo-controlled study, a fixed homeopathic preparation was injected every 5 to 7 days in 20 of 40 patients with steroid-dependent asthma. The treatment group showed a subsequent increase in forced expiratory volume in 1 second, from 1.7 L to 2.4 L versus 1.9 L, declining to 1.8 L in the placebo group. The amount of steroids required by the treatment group also was reduced, from an average of 6 to 3 mg/day [6].

The related problems of pollinosis were addressed in a double-blind study of Galphimia 2_C, which showed a significant improvement of eye and nose symptoms in the treatment group after 2 and 4 weeks [26]. These findings were confirmed in a meta-analysis by the same authors, who summarized seven studies and concluded that there was a significant benefit to Galphimia 2_C use when compared with placebo. This result was similar in effect to antihistamines, but with fewer side effects.

Asthma

A meta-analysis of randomized and possibly randomized trials of homeopathy for the treatment of stable chronic asthma yielded three trials with a total of 154 subjects. All used standardized treatments, which are unlikely to represent common homeopathic practice, in which treatment is individualized. Although two of the three studies showed effects in favor of homeopathy, the authors concluded that there was not enough evidence to recommend homeopathy as a treatment [27].

Influenza

A review of randomized trials on Oscillococinum (a patented homeopathic manufactured from wild duck heart and liver, a well-known reserve

for influenza viruses) in the Cochrane database yielded seven studies for influenza: three prevention trials (n=2265) and four treatment trials (n=1194). There was no evidence that homeopathic treatment prevented influenza, but Oscillocochin treatment reduced the length of illness by 0.28 days and increased the chance that the patient perceived the treatment as effective [28].

Migraine headaches

Homeopaths believe that by stimulating the organism's defense mechanism, they are able to change the established reaction pattern of migraines to a more favorable way of dealing with stress. Seventy-five patients with migraines diagnosed by a neurologist were assigned randomly to either a homeopathic group, or a placebo group. After 1 month, participants were interviewed by a homeopath, and a remedy or placebo was provided. The neurologist reassessed the participants after 5 months. Patient diaries indicated that migraine frequency decreased in both groups, but pain intensity and duration were unchanged. The neurologist's assessments showed 60% of patients in the homeopathic group had fewer attacks, compared with 42% in the placebo group (P=0.04). Pain intensity decreased by 54% in the treated group, versus 42% in the placebo group (P=0.08). Drug consumption decreased in both groups. Although the neurology assessment favored homeopathy, the authors concluded that the main finding was that simply participating in the study reduced the frequency of attacks, pain intensity, and medication consumption [7].

A double-blind, placebo-controlled trial using subjects with chronic headaches showed no benefit of homeopathic treatment compared with placebo, but rather an improvement in both groups of 30%. A follow-up study revealed that the benefits persisted after 1 year, regardless of the treatment allocation [29]. A 1999 systematic review of homeopathic medications in the prophylaxis of migraines concluded that the trial data available to date do not suggest that homeopathy is effective in the prevention of migraines or headaches beyond a placebo effect [30].

Plantar warts

A randomized, double-blind, placebo-controlled trial evaluated the efficacy of a homeopathic treatment of plantar warts. One of four treatments was administered: three homeopathic remedies and one placebo. After 6 weeks of treatment and 18 weeks of follow-up, homeopathy was no more effective than placebo [31].

Joint diseases

Topically administered homeopathy was studied in 184 outpatients with radiographically confirmed symptomatic osteoarthritis of the knee. Patients were entered into a randomized, double-blind, controlled trial and treated with 1 g of a nonsteroidal anti-inflammatory drug (NSAID) in gel form

(piroxicam) or a homeopathic gel three times a week for 4 weeks. Pain reduction, as measured by a visual analog scale, was 16.5 mm in the homeopathic group compared with 8.1 mm in the NSAID group. Adverse events occurred in 12 patients in the homeopathic group and in 16 patients in the NSAID group. The authors concluded that the homeopathic gel was at least as effective and well tolerated as the NSAID gel [32].

A randomized trial on rheumatoid arthritis used 33 patients (17 receiving treatment, 16 receiving placebo) followed for 6 months. Mild benefits were found in both groups, with slightly more benefit in the homeopathy group [33]. In the treatment of acute upper or lower ankle sprains (not graded) in athletes 30 years old and younger (less than 24 hours since injury), 69 patients were randomly assigned to receive either a fixed-combination homeopathic cream or placebo. Of those treated homeopathically, 28 of 36 patients were free of pain on day 10, versus 13 of 33 in the placebo group [2].

Weight loss

One hundred sixty-six moderately obese men (body mass index, 26–35) were treated for 12 weeks with *Helianthus tuberosus* D1. Weight reduction within the treatment group was 7.2 kg versus 4.7 kg in the placebo group ($P < 0.05$) [34].

Meta-analyses

With so much controversy related to individualized trials, meta-analyses may be better able to determine the value of homeopathic treatments.

Kleijnen et al. [10], British Medical Journal

A meta-analysis of 107 controlled trials of homeopathy revealed several good studies, but overall, the methodologic quality was disappointing. In approximately half of the trials (58 studies), the same single homeopathic treatment was given to a group of patients with comparable conventional diagnoses. Evidence was positive, to a large extent: of the better studies, 15 trials showed positive results, whereas in seven trials, no positive effects could be shown. Efficacy of double blinding was not checked (with the patients) in any trial of homeopathy [10].

Linde et al. [35], Lancet

There have been replicated, double-blind, randomized trials showing significant differences between homeopathy and placebo. An odds ratio (OR) of 1.00 indicates no difference between the groups. This meta-analysis showed an OR of 2.45 in favor of homeopathy. Of 186 trials identified, 89 had adequate information to allow statistical meta-analysis. Twenty-six (29%) of these were of high quality. Of all 89 trials, the overall OR was 2.45 (95% confidence interval (CI) 2.05–2.59) in favor of homeopathy. The

OR for the 26 high-quality studies was 1.66 (CI, 1.33–2.08). The general nonparametric selection model that was applied to the 89 studies confirmed a statistically significant publication bias ($P = 0.033$). Correcting for this bias left the OR at 1.78, still substantially and statistically significant. The quality assessment scores suggest that the trials have at least similar quality to those published in the leading medical journals. The authors state that a serious effort to research homeopathy clearly is warranted despite its implausibility. They concluded that, even allowing for publication bias, “the results of our meta-analysis are not compatible with the hypothesis that the clinical effects of homeopathy are completely due to placebo” [35].

Cucherat et al. [36], European Journal of Clinical Pharmacology

A meta-analysis using randomized, placebo-controlled clinical trials with a defined endpoint as the selection criteria examined 16 trials, which represented 17 comparisons and included a total of 2617 evaluated patients. The P value tended toward a nonsignificant value ($P = 0.08$), because trials were excluded in a stepwise manner based on their level of quality. The authors concluded that although there is some evidence that homeopathic treatments are more effective than placebo, the strength of this evidence is low because of the low methodologic quality of the trials [36].

Studies in children

The low toxicity rates reported with homeopathic medications help lend support to the use of these preparations in children. Children aged 6 months to 5 years with mild to moderate diarrhea had a 15% reduction in duration of symptoms (0.8 days) compared with placebo, after being randomly assigned to one of 18 homeopathic medications chosen on the basis of a complete homeopathic interview. The OR was 2.7, in favor of homeopathy. If the diarrhea was found to be caused by pathogens, the homeopathic treatment was better than placebo ($P = 0.006$). There was no significant difference in nonpathogenic diarrhea [4]. In a study with infants with Rous sarcoma virus, daily injection of a homeopathic combination remedy showed some improvement after 5 days of treatment versus a placebo group and complete resolution of symptoms after 14 days in all treated infants, versus 89% of the placebo group [37].

Side effects

Unwarranted effects are not reported routinely in homeopathic trials. There is some anecdotal evidence for allergic reactions [38]. In a meta-analysis of the adverse effects of homeopathic medicines, the mean incidence of adverse effects of homeopathic medicines was greater than placebo in controlled clinical trials, but effects were minor and transient. Case reports

in conventional medical journals pointed more to adverse effects of mis-labeled homeopathic products than to true homeopathic medicines. Homeopathic medicines in high dilutions, prescribed by trained professionals, are safe and unlikely to provoke severe adverse reactions. The most common effects were headaches, tiredness, skin eruptions, dizziness, bowel dysfunctions, and symptom aggravation. These effects were not different from the effects noted in placebo groups in clinical trials [39].

Cost

Homeopathic medications are inexpensive (approximately \$5 per container); currently consumers in the US are spending approximately \$200 million per year homeopathic medications. Although less expensive than allopathic drugs, proper evidence should be considered before using these medications.

Obstacles in conducting research on homeopathy

There are some inherent difficulties in trying to apply the standard randomized, placebo-controlled paradigm to homeopathic remedies. Assumptions that one model of treatment will fit across all therapies may be inapplicable to homeopathy. There is a lack of evidence that homeopathy is clearly efficacious for any single condition, but the weight of anecdotal evidence must count for something [40].

Future directions

Clearly, high-quality, well-controlled studies are needed before homeopathy attains credibility in the allopathic world. With more alternative practitioners becoming trained to perform drug studies, it is hoped that this will become a reality.

If homeopathy's effect can be established beyond a doubt, qualifications of prescribers need to be evaluated. The complex medications given for specific narrow indications do not require much depth of knowledge; however, finding the exact individualized remedy requires substantial homeopathic training and experience. Although computer programs have been used effectively in randomized clinical trials, their use without knowledge of the homeopathic interview is not recommended.

A search of the National Center for Complementary and Alternative Medicine web site revealed that of the \$70 million allocated to the center, only one study has been funded that implements homeopathy as a treatment. Without funding, the likelihood of quality trials may remain small. Future, well-conducted, randomized trials are essential for accepting homeopathy as a mainstream medicine.

Conclusions

Homeopathy has intrigued the Western world for more than 150 years. Although many of the trials point to an effect when compared with no treatment or placebo, further studies are necessary to elucidate specific indications for rational use.

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