

Homeopathic Medicine and Symptoms of Restless Legs

Overview of Homeopathy

Homeopathy is a 200-year-old system of complementary and alternative medicine (CAM) developed by the German physician Samuel Hahnemann, MD. More than 500 million people worldwide have used homeopathic remedies (Kaul, 1996). Homeopathy is an established and widely available form of health care in countries such as the U.K., Germany, France, Belgium, Switzerland, Netherlands, India, and across Latin America. Homeopathy in the U.S. has undergone a cyclical course. In the early 1900's, there were reportedly 22 homeopathic medical schools (originally including institutions such as Boston University and New York Medical College), 100 homeopathic hospitals, over 1000 homeopathic pharmacies across the U.S. Disputes between physicians in the American Medical Association and the American Institute of Homeopathy led to the decline of homeopathy in the U.S. until its resurgence in the latter part of the 20th century.

In the U.S., large-scale national surveys have shown that the percentage of adults reporting use of homeopathy in the past 12 months has grown from 0.7% in 1990 to 3.4% in 1997 (Eisenberg, 1998), with continued annual growth. Reasons for trying homeopathy among users from the CDC-based report from the 2002 National Health Interview Survey (Barnes, Powell-Griner, McFann, & Nahin, 2004) included 43% expecting the combination of conventional and homeopathic treatment would help; 36.7% indicating that conventional medical treatments would not help their condition; and 19.4% stating that conventional medical treatments were too expensive. Consumers use homeopathy both for self-care and under practitioner supervision.

In homeopathy, the mental, emotional, and/or physical symptoms that a patient presents lead to selection of a medicine (remedy) to treat the patient as a whole. Homeopathic medicines are manufactured from natural animal, mineral, and plant sources. The source material is crushed in lactose and/or extracted and dissolved in a water-alcohol solvent. Remedy preparation involves serial dilution and succussion (vigorous shaking) of the source material, commonly by factors of 10 (decimal series, X) or 100 (centesimal series, c) to 1 in distilled water. Thus, a 12X remedy has been diluted $(1/10)^{12}$ and succussed 240 (or more) times. The final remedy is often stabilized by addition of small amounts of pharmaceutical-grade ethanol and formulated in dissolvable pellets or tablets containing lactose and/or sucrose for ease of oral administration. Unlike many dietary supplements such as herbs, the preparation of homeopathic remedies is standardized in published monographs from the Homeopathic Pharmacopoeia of the U.S. (see Legal/Regulatory Status below).

Consumers use single or mixtures of homeopathic over-the-counter remedies for self-care first aid in injuries (Oberbaum, Schreiber, Rosenthal, & Itzchaki, 2003) or acute illnesses such as colds and flu (Vickers, 2006). Many times the remedies appear to shorten the duration of the acute illness or speed up the recovery process. For treatment of many persons with a wide range of chronic symptoms, constitutional homeopathic treatment involves a highly trained and experienced practitioner to select the correct treatment with a single remedy at a time and manage the case in partnership with the patient over a period of months to years. However, many consumers manage their own intercurrent symptoms using over-the-counter remedies as part of their self-care.

Legal/Regulatory Status of Homeopathic Medicines as Drugs

Homeopathic medicines have been considered to be drug products under the law since the inception of the Federal Food, Drug and Cosmetic Act ("FD&C Act"), 21 U.S.C. § 201 et seq.,

sponsored by Senator Royal Copeland, M.D., himself a homeopathic physician, in 1938. Section 201(g)(1) of the FD&C Act, 21 U.S.C. § 321(g)(1), defines the term "drug" to include "articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary,[1][1]/ or any supplement to any of them" (Emphasis added.)

Section 201(j) of the Act, 21 U.S.C. § 321(j), defines the term "official compendium" as the "official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States (HPUS), official National Formulary or any supplement to any of them" (Emphasis added.)

On June 9, 1988, the Food and Drug Administration announced in the Federal Register, 53 Fed. Reg. 21728, the availability of Compliance Policy Guide 7132.15, "Conditions Under Which Homeopathic Drugs May be Marketed." The Compliance Policy Guide "provides guidelines on the regulation of OTC and prescription and homeopathic drugs and describes those conditions under which homeopathic drugs may ordinarily be marketed in the U.S." The Guide reiterates the statutory declaration of the HPUS as an official compendium under Section 201(j) of the Act, and recognizes the homeopathic status of any drug which is listed in the HPUS.

It is important to remember that since homeopathic medicines are classified as drugs and since they are subject to both the conventional drug regulations and the HPUS, they are fairly highly regulated. From the perspective of manufacturing and marketing, homeopathic products (unlike other forms of CAM), are regulated in substantially the same manner as their conventional counterparts. The Compliance Policy Guide also identifies the homeopathic materia medica which can be used to develop indications for homeopathic products.

Homeopathic Research Summary

Observational studies on thousands of patients with a wide variety of health conditions show a consistently high rate of patient improvement (70-80%) and high patient satisfaction with homeopathic treatment, with significantly lower rates of adverse events than with conventional drugs (Bornhoft, 2006; Goldstein, 1998; Riley, Fischer, Singh, Haidvogel, & Heger, 2001; Schlappack, 2004; Sevar, 2000, 2005; Thompson, 2002; van Wassenhoven & Ives, 2004; C. Witt et al., 2005; C. M. Witt, Luedtke R, Baur R, Willich SN., 2005). In some, but not all studies, the inclusion of homeopathy in an integrative medical treatment program led to significantly reduced costs for conventional drugs (Frenkel & Hermoni, 2002; van Wassenhoven & Ives, 2004).

Skeptics continue to insist that homeopathy is nothing more than placebo (Lancet, 2005; Weissmann, 2006). Despite the recent emphasis on evidence-based health care, skeptics, however, fail to mention extensive basic science, animal, and preclinical data showing that homeopathic remedies are not placebos (Brizzi, Nani, Peruzzi, & Betti, 2000a, 2000b; Datta, Mallick, & Bukhsh, 1999; Jonas, Lin, & Tortella, 2001; Kundu, Mitra, & Khuda Bukhsh, 2000; D. Marotta et al., 2002; D. Marotta, Marini, A, Banaudha, K., Maharaj, S., Jonas, W.B., 2003; Mitra, Kundu, & Khuda Bukhsh, 1999) (Bell, Lewis, Lewis et al., 2004; Belon, 2004; Belougne-Malfatti, Aguejouf, Doutremepuich, Belon, & Doutremepuich, 1998; Bertani, Lussignoli, Andrioli, Bellavite, & Conforti, 1999; Biswas & Khuda-Bukhsh, 2004; Doutremepuich, Aguejouf, Pintigny, Sertillanges, & De Seze, 1994; Lussignoli, Bertani, Metelmann, Bellavite, & Conforti, 1999; MacLaughlin et al., 2006; A. Sukul, Sinhabau, & Sukul, 1999; N. C. Sukul, Bala, S.K., Bhattacharyya, B., 1986; N. C. Sukul, Ghosh, Sinhababu, & Sukul, 2001).

The body of evidence from animal, plant, and controlled clinical trials show that homeopathic remedies exert measurable biological effects, though in ways not identical to conventional drug actions and not necessarily in linear dose-response patterns. Nonlinear, including bidirectional, dose-response patterns are a well-documented phenomenon in the hormesis literature within conventional toxicology for agents ranging from radiation to pesticides/herbicides to various pharmaceutical drugs (E. J. Calabrese, 2005; E. J. Calabrese, Baldwin, L.A., 2001). Hormesis, which involves nonlinear dose-response relationships such as reversal in the direction of effects of an agent in going from high to low doses, is more often reported at doses below the lowest observed adverse effect level in toxicology, i.e., below toxic threshold levels (E. J. Calabrese, 2005; E. J. Calabrese & Baldwin, 2000; E. J. Calabrese, Baldwin, L.A., 2001). The preparation process for homeopathic remedies generally places the doses close to or below the lowest observed adverse effect level for a given substance (Mallick, Chakrabarti, Guha, & Khuda-Bukhsh, 2003).

At the same time, the succussion of remedies introduces persistent and measurable changes in the materials science properties of the solvent that are not seen with simple serial dilution by itself (Elia, 1999, 2004; Rey, 2003; Roy, Tiller, Bell, & Hoover, 2005). The data from calorimetric and thermoluminescence studies demonstrate properties of homeopathic remedies that are not identical to “placebo” or unsuccessed solvents with dissolved materials simply stirred into the liquid. How remedies interface with living systems is not well-studied or understood. Recent models of remedy action propose that the remedy stimulates or catalyzes self-healing properties of the individual organism as a living nonlinear dynamical complex system with the capacity for self-organization (Bell, Baldwin, & Schwartz, 2002; Bell & Koithan, 2006; P. Bellavite, 2003; P. Bellavite, Signorini, A., 2002; M. Hyland, 2003; M. E. Hyland & Lewith, 2002; Milgrom, 2002; Torres, 2002). Similarly, hormetic (low) doses of conventional drugs appear to stimulate the capacity of the host to counteract the adverse, toxic effects of the same drug at higher doses.

Controlled clinical trial studies supporting homeopathy as a possible treatment include patients with not only childhood diarrhea (J. Jacobs, Jimenez, Gloyd, Gale, & Crothers, 1994; J. Jacobs et al., 2000; J. Jacobs, Jonas, Jimenez-Perez, & Crothers, 2003), otitis media (Harrison, Fixsen, & Vickers, 1999; J. Jacobs, Springer, D.A., Crothers, D., 2001), attention deficit-hyperactivity disorder (H. Frei, Everts R, von Ammon K, Kaufmann F, Walther D, Hsu-Schmitz SF, Collenberg M, Fuhrer K, Hassink R, Steinlin M, Thurneysen A., 2005; H. Frei, Thurneysen A., 2001; H. Frei, von Ammon, & Thurneysen, 2006; Lamont, 1997), fibromyalgia (Bell, Lewis, Brooks et al., 2004; P. Fisher, Greenwood, A., Huskisson, E.C., Turner, P., Belon, P., 1989), and chemotherapy-induced stomatitis (Oberbaum et al., 2001), but also life-threatening medical conditions such as sepsis (Frass et al., 2005). In the latter ICU study upon 180 day followup, survival rates of patients treated with adjunctive homeopathy in combination with conventional care were significantly higher (75.8%) than those of septic patients treated with conventional care alone (50%)($p=0.043$).

Most of the meta-analyses of homeopathic clinical trials have been flawed methodologically (Shang, 2005), including study selection, limited numbers of available studies in any one allopathic diagnosis, and methodological errors from a conventional perspective (Aickin, 2005; P. Fisher, Berman B, Davidson J, Reilly D, Thompson T. , 2005). The majority of meta-analyses nonetheless have favored homeopathy overall versus placebo (Cucherat, Haugh, Gooch, & Boissel, 2000; Linde et al., 1997; Reilly, 1994). In addition, no meta-analyses of homeopathy have included any quality ratings for the homeopathy itself as delivered during a study, as a criterion for including the study in the analysis. No meta-analyses have included any assessment of outcomes based upon theory-driven hypotheses from a homeopathic

perspective, in which patterns of multiple symptom outcomes are expected, rather than only focal changes in a specific body part or treatment of a specific disease.

Homeopathy in Persons with Symptoms of Restless Legs

Homeopathic remedies, including OTC combination medicines, are not formulated to treat allopathic diagnostic disorders. Rather, indications for remedies are based upon historical documentation in the homeopathic material medica, in which specific, widely-used remedies have been reported to alleviate certain symptoms. Persons experiencing symptoms of restless legs complain of crawling or cramping feelings in the legs, worse in the evening and at night, with an urge to move. In accord with regulatory guidelines for combination homeopathic medicines and as outlined in the Homeopathic Pharmacopoeia of the U.S., Hyland's Restful Legs product includes the following homeopathic plant and mineral remedies with the specific symptom indications:

Remedy and Homeopathic Dose Potency	Symptom Indication
Arsenicum Album 12X, HPUS	Creeping, crawling itch
Lycopodium 6X, HPUS	Restless legs, while lying down
Pulsatilla 6X, HPUS	Constant urge to move legs
Rhus Toxicodendron 6X, HPUS	Restless legs, better with activity
Sulphur 6X, HPUS	Itching, tingling, urge to move legs
Zinc Metallicum 12X, HPUS	Twitching and jerking of legs, while sitting

Each remedy in the combination product addresses the symptoms listed to its right in the table. Notably, each of the remedies in the Restful Legs product is a widely-used and well-documented homeopathic remedy with decades and even up to 200 years of safe use in infants, children, and adults. When adverse effects of homeopathic treatment have been reported, the nature of the effects has been transient and typically consists of a temporary increase in symptoms that the patient has previously experienced. Once this transient "aggravation" resolves, patients improve over time rather than experience recurrent worsenings (in contrast with the progressively worsening symptom rebounds seen with dopaminergic drugs over time).

When used as directed, emergent adverse symptoms from homeopathic medicines that the patient has never experienced previously, unlike conventional drug side effects, are rare. The type of temporary symptom increase is also reported in non-drug CAM therapies such as acupuncture, which, like homeopathy, has an overall excellent safety record in the available literature. Although homeopathic medicines are considered a unique class of drug in a regulatory sense, these agents do not cause drug-drug interactions.

Homeopathic medicines do not exert the kinds of pharmacokinetic or pharmacodynamic effects seen with conventional medications. Homeopathic medicines used as directed do not lead to the same kinds of adverse side effects seen commonly with conventional dopaminergic agents, such as nausea, vomiting, drowsiness, irresistible sleepiness, low blood pressure and syncope, and hallucinations. In fact, because of the apparent ability of homeopathic medicines to trigger healing within the individual without continuous dosing, instructions for use of homeopathic medicines are to take doses until symptom improvement begins - and then to discontinue use unless and until any symptoms return.

Consequently, the main risks of adverse effects with homeopathic medicines, while much lower than those of conventional drugs, would consist of initial and temporary increases in symptoms of restless legs, not the appearance of new symptoms. However, in contrast with conventional

dopaminergic agents in which rebound worsening of symptoms is a fairly common occurrence, with the likelihood of recurring and even progressively worse problems, the transient symptom increases after initial dosing with a homeopathic medicine lead to sustained subsequent improvement in the typical case. Moreover, none of the homeopathic medicines in Restful Legs is addictive, thereby avoiding the risk of physical and/or psychological dependence that benzodiazepines and opioids, which are sometimes used as an alternative medication to dopaminergic agents (Clark, 2001), usually pose.

Conclusions

The symptoms of restless legs substantially impair quality of life for affected persons (Garcia-Borreguero, Egatz, Winkelmann, & Berger, 2006; Lopes et al., 2005; Merlino, Valente, Serafini, & Gigli, 2007). Individuals with idiopathic symptoms of restless legs and those with restless legs symptoms secondary to end-stage renal disease, iron deficiency, and perhaps diabetes mellitus type II are often already compromised with polypharmacy treatment and risks of adverse conventional drug reactions and interactions. Homeopathic treatment offers the option for patients to use a well-regulated form of complementary and alternative medicine with a documented history of greater safety in widespread use among the general population and among patients with chronic and acute illnesses, even individuals compromised by life-threatening sepsis, as compared with many conventional drugs.

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