

ORIGINAL RESEARCH

Homeopathic Medications as Clinical Alternatives for Symptomatic Care of Acute Otitis Media and Upper Respiratory Infections in Children

顺势疗法药物作为儿童急性中耳炎和上呼吸道感染对症护理的临床替代药物

Medicamentos homeopáticos como alternativas clínicas para la atención sintomática de la otitis media aguda y de la rinofaringitis (infección respiratoria de las vías respiratorias altas) en niños

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ABSTRACT

The public health and individual risks of inappropriate antibiotic prescribing and conventional over-the-counter symptomatic drugs in pediatric treatment of acute otitis media (AOM) and upper respiratory infections (URIs) are significant. Clinical research suggests that over-the-counter homeopathic medicines offer pragmatic treatment alternatives to conventional drugs for symptom relief in children with uncomplicated AOM or URIs. Homeopathy is a controversial but demonstrably safe and effective 200-year-old whole system of complementary and alternative medicine used worldwide. Numerous clinical studies demonstrate that homeopathy accelerates early symptom relief in acute illnesses at much lower risk than conventional drug approaches. Evidence-based advantages for homeopathy include lower antibiotic fill rates during watchful waiting in otitis media, fewer and less serious side effects, absence of drug-drug interactions, and reduced parental sick leave from work. Emerging evidence from basic and preclinical science research counter the skeptics' claims that homeopathic remedies are biologically inert placebos. Consumers already accept and use homeopathic medicines for self care, as evidenced by annual US consumer expenditures of \$2.9 billion on homeopathic remedies. Homeopathy appears equivalent to and safer than conventional standard care in com-

parative effectiveness trials, but additional well-designed efficacy trials are indicated. Nonetheless, the existing research evidence on safety supports pragmatic use of homeopathy in order to "first do no harm" in the early symptom management of otherwise uncomplicated AOM and URIs in children.

背景

在对急性中耳炎 (acute otitis media, AOM) 和上呼吸道感染 (upper respiratory infections, URI) 的小儿科治疗中, 不适当的抗生素处方药和传统的非处方症状性药物所引起的公共卫生和个体风险是显著的。临床研究表明, 在缓解患有无合并症 AOM 或 URI 之儿童的症状方面, 非处方顺势疗法药物可作为传统药物的实际治疗替代方案。顺势疗法是一种存有争议但确实安全有效的治疗方法, 作为完整的补充和替代医疗方法, 在全球范围内已有 200 年的应用历史。大量临床研究表明, 顺势疗法可加速急性疾病的早期症状缓解, 且风险远远低于传统药物方法。顺势疗法有据可循的优点包括降低中耳炎观察等待期间的抗生素供应率, 减少并缓解严重副作用, 减少药物间相互作用和减少亲子病假。基础和临床前科学研究新近得出的证据驳斥了持怀疑观点人士所持有的主张, 即顺势疗法就是生物学上的不活泼安慰剂。美国消费者每年 29 亿美元的顺势疗法支出, 证明了消费者已经接受并使用顺势疗法药物来进行自我护理。在多项比较效果试验中, 顺势疗法似

乎与传统标准护理具有同等效果, 并且更加安全, 但仍需要进行更多项精心设计的效力试验。虽然如此, 但为了在患有其他无合并症 AOM 和 URI 之儿童的早期症状管理方面做到“首先无害”, 现有的安全性研究证据支持在实际生活中采用顺势疗法。

SINOPSIS

La salud pública y los riesgos individuales de la receta inapropiada de antibióticos y de los fármacos sintomáticos sin receta tradicionales en el tratamiento pediátrico de la otitis media aguda y de las infecciones de las vías respiratorias superiores son importantes. La investigación clínica indica que los fármacos homeopáticos sin receta ofrecen alternativas pragmáticas de tratamiento a los fármacos tradicionales para el alivio de los síntomas en niños con otitis media aguda o infecciones de las vías respiratorias superiores sin complicaciones. La homeopatía es un completo sistema de medicina alternativa y complementaria que lleva utilizándose 200 años en todo el mundo y, aunque controvertida, ha demostrado ser segura y eficaz. Numerosos estudios clínicos demuestran que la homeopatía acelera el alivio temprano de los síntomas en las enfermedades agudas con un riesgo muy inferior a los enfoques farmacéuticos tradicionales. Las ventajas basadas en las pruebas para la homeopatía incluyen unas tasas de relleno de antibióticos inferiores durante la espera con vigilancia en la

otitis media, menos efectos secundarios y de menor gravedad, ausencia de interacciones entre los fármacos y reducción de los permisos laborales por enfermedad de los padres. Las pruebas que surgen a partir de la investigación científica básica y preclínica desmienten las afirmaciones de los escépticos que indican que los remedios homeopáticos son placebos biológicamente inertes. Los con-

sumidores ya aceptan y utilizan fármacos homeopáticos para su propio cuidado, según lo prueban los gastos anuales en Estados Unidos con un consumo de 2900 millones de dólares en remedios homeopáticos. La homeopatía parece corresponderse y ser más segura que la atención tradicional estándar en los ensayos comparativos de eficacia, pero se indica la realización de ensayos adi-

cionales sobre eficacia bien diseñados. No obstante, las pruebas existentes derivadas de la investigación sobre seguridad apoyan el uso pragmático de la homeopatía para, en primer lugar, «no causar daño» en la gestión y tratamiento tempranos de los síntomas de la otitis media aguda y las infecciones de las vías respiratorias superiores sin complicaciones en niños.

The common practice of inappropriate antibiotic prescribing in otherwise self-limited pediatric illnesses such as acute otitis media (AOM) and upper respiratory infections (URIs) has increased public health risks of treatment-resistant organisms.¹ Conventional symptomatic over-the-counter (OTC) drugs also carry their own side effect risks, including anticholinergic toxicity² or liver injury from accidental overdoses.^{3,4} As an alternative, this article presents a clinically focused, evidence-based perspective on the rationale for using homeopathic medicines for symptomatic treatment of acute, uncomplicated illnesses such as colds, flu, and otitis media in children.

Homeopathy is a controversial 200-year-old whole system of complementary and alternative medicine (CAM) used worldwide, with an excellent safety track record.⁵ Although skeptics reject homeopathy as chemically “implausible,”⁶ newer evidence on the physico-chemical⁷⁻¹⁵ and nanoparticulate¹⁶⁻¹⁹ properties of homeopathic medicines and on adaptive nonlinear responses of living systems to low-dose treatments²⁰⁻²⁶ casts doubt on the simplistic dismissal of the entire field. Furthermore, a growing body of clinical evidence, including comparative effectiveness trials on thousands of homeopathic patients, a strong safety record, and cost-effectiveness data, make homeopathy a therapeutic strategy that merits consideration.^{5,27-31} Primary care clinicians who wish to learn more about how to use homeopathic medicines for acute pediatric care can find multiple introductory resources online³² and in the print media.³³⁻³⁵

A significant challenge in outpatient pediatric care is the treatment of symptoms³⁶ from acute infections, fevers, mild allergic reactions with rhinitis or pruritis, and minor injuries. For example, a recent survey showed that sore throat/strep throat, sinus infections, URIs, common colds/fever, ear infections, and coughs are the top six types of conditions across all ages of patients treated by approximately 200 retail clinic-based health practitioners.³⁷ Most common acute viral illnesses and some bacterial infections are, by definition, self-limited within a short time period. Consequently, the relative benefits of any intervention must far outweigh the risks to justify its use in an otherwise healthy child who develops symptoms of AOM or a URI.

CURRENT CLINICAL MANAGEMENT OF ACUTE PEDIATRIC ILLNESSES: LIMITATIONS AND RISKS

For instance, antibiotics carry risks of causing diarrhea and allergic reactions, as well as antibiotic resistance.³⁸⁻⁴² In otitis media, clinical watchful waiting guidelines from the American Academy of Pediatrics suggest that the condition will resolve in many children without antibiotic intervention (<http://www.aafp.org/afp/20000415/2410.html>).^{43,44} Antibiotics confer only a small benefit in this common primary care scenario.⁴³ It often remains a clinical judgment as to how and when to draw a line between possible/uncertain otitis without severe illness meriting a watch-and-wait strategy and definite otitis media with “severe illness” in a child requiring immediate antibiotic treatment. Many health-care providers and parents still end up choosing to fill the antibiotic prescriptions and accept the associated risks,³⁹ presumably out of a wish to do something rather than nothing while a child is distressed and suffering.^{45,46} Moreover, many providers still give a non-evidence-based prescription of antibiotics in likely viral infections^{1,39} from which only placebo effects could be expected along with the short-term (diarrhea, allergic reactions) and long-term (increasing antibiotic resistance) risks from unnecessary antibiotic usage.⁴² In fact, a recent analysis of ambulatory pediatric practice survey data from 2006 to 2008 in the United States revealed that despite a lack of clear indications, 23% of visits for respiratory conditions nonetheless led to antibiotic prescriptions (ie, >10 million visits annually).¹

Furthermore, commonly used OTC symptom-relief medications include products containing acetaminophen or ibuprofen, as well as various antihistamines such as diphenhydramine or chlorpheniramine. Cough syrups include ingredients such as dextromethorphan, and decongestant cough and cold relief formulations may also contain guaifenesin and phenylephrine. Some products are now contraindicated in children under 4 years old, leaving parents with very limited choices for relieving a young child’s symptoms during the common acute infections that children in that age group often develop. Most of these drugs have significant rates of common side effects, such as dry mouth, gastrointestinal upsets, or excessive sleepiness.

However, these OTC conventional symptomatic drugs also cause less common but potentially even life-

Table 1 Common Pediatric Medications Used for Upper Respiratory Infections and Otitis Media Symptoms

Medication	Side Effect Risks	Less Common but Serious Adverse Events
Acetaminophen	Increased risk of asthma ⁴⁷	Liver damage in overdose
Ibuprofen	Gastrointestinal bleeding	Severe blood loss, gastrointestinal ulcers
Diphenhydramine Chlorpheniramine	Anticholinergic toxicity—including blurry vision, dry mouth, tinnitus, drowsiness, dizziness. Antihistamines are the 8th most common exposure among children younger than 5 y (2008 National Poison Data Center ⁴)	Urinary retention, cardiac dysrhythmias, seizures, apnea, agitation, rhabdomyolysis. Severity of adverse effects not necessarily related to dose ingested in children with single accidental dose ² Antihistamines cause moderate to major toxicity in 3.6% of all reported exposures to poison control centers (2007) and 0.09% fatalities ⁴
Dextromethorphan	Blurry vision, confusion, difficulty urinating, drowsiness, dizziness, nausea and vomiting, poor balance, slowed breathing, paradoxical excitement or agitation	
Guaifenesin	Headache, nausea, vomiting	
Phenylephrine decongestant	Trembling, sweating and rapid irregular heartbeat, anxiety, nervousness, dizziness, insomnia Dryness in nose, difficulty urinating, bleeding or bruising, weakness or fainting	Severe allergic reactions Side effects more severe in children
Antibiotics (eg, amoxicillin)	Diarrhea (up to 47.8% rate in children treated for definite otitis media) ^{41,48} Diaper dermatitis ⁴¹	Anaphylaxis and other allergic reactions Antibiotic resistant infections from inappropriate excessive use ⁴⁹

threatening risks of serious adverse events. Table 1 lists the scope of possible side effect risks of such conventional medications. Unintentional parent-caused overdoses due to lack of symptom relief is also a worry. Of concern, one of the most commonly used antihistamine drugs, diphenhydramine, can cause adverse events from a single accidental ingestion without a linear dose-response relationship.² Taken together, the evidence suggests that finding alternatives for symptom relief with lower risks than conventional drugs for children in the setting of uncomplicated URIs, otitis media, and/or mild allergies is highly desirable.⁵⁰

HOMEOPATHIC MEDICINES AS ALTERNATIVE INTERVENTIONS

Homeopathy was originally developed by the German physician-chemist Samuel Hahnemann, MD, out of concerns about the toxicity of available treatments for acute and chronic illnesses of his day.⁵¹ Although the term “homeopathy” is often misunderstood in conventional circles as a generic definition of all forms of alternative medicine including herbal medicines, homeopathy is quite distinct from other forms of conventional drugs, herbs, and other natural supplements.

Homeopathic medicines are manufactured from natural animal, mineral, and plant substances with a specific set of procedures, including extensive grinding and repeated serial dilutions followed by succussions (vigorous shaking or agitation against a hard surface). The dilution factors are described in most cases as 1/10 dilution ratio steps (X series) or 1/100 dilution ratio steps (C series). For example, a 30C “potency” of a homeopathic medicine has been diluted to achieve a

bulk form concentration of 100⁻³⁰ over 30 consecutive steps, each using a ratio of 1 part of the diluted source material to 100 parts solvent (typically ethanol-water). The medicine is also succussed multiple times after each dilution step, (eg, 20 times per dilution step), a process that multiple studies have shown releases measurable amounts of silica and its precursors into solution from the glass containers.^{15,19,52}

The manufacturing process thereby dilutes the bulk form source material at a 100⁻³⁰ factor and succusses it for a total of 600 times (ie, 20 succussions per dilution step, repeated 30 times). Studies from multiple laboratories have now demonstrated that homeopathically prepared medicines, even in ultra dilute bulk form doses, have unique, measurable physico-chemical properties not found in placebos or control solvents.^{7,9-13,15,16,53,54} Trituration and/or succussion steps appear to be necessary to make a homeopathic remedy.^{14,55,56} Thus, dilution by itself, although the focus of most skeptics, is not sufficient to make a homeopathic medicine biologically active at low dose.⁵⁷

Some key distinctions between homeopathic medicines and bulk form conventional drugs or other natural products include the following.

- The classical homeopathic manufacturing procedures of mechanical grinding (trituration) and dry dilution in lactose and/or serial liquid dilutions of source material (mineral, plant, animal) using ethanol-water in glass vials, followed by multiple succussions (intense manual shaking, pounding against a hard surface or turbulence from vortexing or sonication in the solution) would generate

increasingly smaller particles broken off from the source material by collisions and shearing forces.⁵⁷ In modern nanotechnology, these types of procedures generate “top-down” nanoparticles (NPs) from bulk form source materials.⁵⁸⁻⁶³ In fact, source NPs have been demonstrated to be present in low concentrations of metal homeopathic remedy dilutions at 6C, 30C, and 200C¹⁶ and plant remedy dilutions at 1C to 15C.¹⁹ Homeopathic or herbal plant mother tinctures can also biosynthesize silver, gold, or silica NPs, with biological properties modified by the specific plant source.⁶⁴⁻⁶⁷

- As NPs, homeopathic remedies acquire unique electromagnetic, thermal, optical, chemical, catalytic, adsorptive, biological, and quantum properties by virtue of their small size, with high surface area to volume ratios.^{67,68} At nontoxic doses, silica NPs, for instance, can amplify the biological and immune effects of natural substances⁶⁹ and/or antigens.⁷⁰ Different from their respective bulk forms, NPs are highly bioavailable, cross membranes easily, and activate the biological stress system pathways of the body.^{67,71-74} NPs are extremely adsorptive onto their large surface areas and can also self-assemble larger ordered structures,⁷⁵ even contributing to peptide self-assembly in experimental tissue repair.⁷⁶ NPs lower side effects and the doses of agents, including herbs, needed to elicit a given effect.^{66,77-80} Moreover, NPs can cause adaptive hormesis (beneficial stimulation) at very low doses.^{22,81}
- Homeopathic products labeled as “HPUS” are prepared in accord with standardized procedural monographs documented in the official Homeopathic Pharmacopoeia of the United States (HPUS: www.HPUS.com) and are carefully tested to ensure that the correct amounts of intended ingredients are present and that no contaminants or adulterants are included in the products. Other countries also maintain their own official homeopathic pharmacopoeias and standards as well (eg, United Kingdom, Germany, India).
- In the United States, homeopathic medicines are regulated as drugs by the US Food and Drug Administration, whereas OTC herbal supplements are subjected to a lesser standard.
- Homeopathic medicines are not reported to cause drug-drug or drug-herb interactions, in contrast with the risks of common OTC conventional drugs and herbal supplements.⁵
- Homeopathic doses are very small, but the clinical evidence is that they can be effective.^{5,29} The way in which they act is not necessarily by the same local receptor mechanisms as conventional drugs or herbs.^{17,29,82,83}

- Rather, many doses of homeopathic medicines appear to stimulate adaptive changes of plasticity in regulatory systems of the body as a complex system⁸⁴⁻⁸⁸ that result in a nonlinear reversal in direction of symptoms.^{21,23,89-92} The positive adaptive (hormetic) dose levels typically fall below the no-observed-adverse-effects level (NOAEL) from a toxicology perspective.^{82-85,93-97}
- A basic principle is that the homeopathic medicine stimulates the body’s own adaptive healing processes (ie, the postexposure conditioning component of hormesis^{21,25}) and/or bidirectional effects of low dose sensitization.^{98,99}
- Mechanisms may include NP-induced activation of inflammasomes,⁷¹ heat shock proteins,^{21,25,100} neuroendocrine sensitization¹⁰¹⁻¹⁰³ pathways, other biological signaling pathways,¹⁰⁴ exosomes, and/or reticuloendothelial system mobilization of systemic immune responses.⁷²
- The ways in which homeopathic remedy NPs could signal the host organism of their presence include biochemical,^{21,25,67} electromagnetic¹⁰⁵ and magnetic⁶⁸ signals, as well as optical¹⁰⁶ or quantum macro entanglement effects.¹⁰⁷
- These nonlinear, natural effects depend on the body, not the medicine, to do the work.^{90,91,108} To exert these effects, a homeopathic medicine must be salient to the overall, integrated symptom pattern that the individual expresses as a complex system.^{84,85} A non-salient medicine selection will fail to interact therapeutically with the individual.^{109,110}

The clinical selection of the homeopathic medicine is based on the totality of the symptom pattern or picture that the patient presents.⁵¹ Thus, three patients with the “same” conventional medical diagnosis could receive three different homeopathic medicines and experience benefit. Combination homeopathic medicines sold over the counter for self-care may contain two to six or more individual medicines, with the goal of addressing the most common acute symptoms that most people in a given patient population might experience at some point in the course of their illness. Thus, primary care clinicians have the option of learning how to select from a small number of individual homeopathic remedies for pediatric AOM or URIs³⁴ or recommending a combination remedy product containing the most often used remedies together. The relatively small total pool of possible appropriate homeopathic medicines for acute illnesses numbers in the range of 50 to perhaps 100 individual remedy possibilities, thus making acute homeopathic medicines a feasible treatment strategy for primary care clinicians.

ADVANTAGES OF HOMEOPATHIC MEDICATIONS

Overview

The human body, like any living system, is a complex adaptive network of component interactive and self-organizing networks.^{85,111,115} Among these networks, the body's biological stress response "allostatic" network uses immune, inflammatory, metabolic, endocrine, and nervous system pathways to adapt to environmental change, self-regulate, and maintain the internal milieu for survival.^{116,117} The core advantage of homeopathic medicines over conventional drugs is that the homeopathic agents stimulate the body to heal itself globally from within. That is, each discrete dose of the remedy interfaces with components of the stress response network^{21,25,87,100} as a salient mild stressor to initiate systemic self-reorganization toward more robust functioning as a whole integrated network.^{87,88,90,91,94,113} In contrast, most conventional medicines focus on either killing an exogenous infectious organism or suppressing specific local manifestations of disease. Conventional drug "side effects" can impose additional disturbances to which the body must also adapt while still dealing with the underlying condition.⁹¹ Moreover, the infectious organism itself begins to evolve its own adaptations to survive by developing drug resistance.

At a practical level, homeopathy offers several other advantages over conventional OTC symptomatic drugs for acute pediatric care: (1) fewer and less serious side effects, (2) earlier onset symptom improvements, and (3) lower costs, with reduced use of conventional symptomatic drugs.⁵

Safety

There are no definite contraindications to acute or chronic use of homeopathic medicines in children other than those with extreme sensitivity or allergy to a source material still present in trace amounts in the lower potency homeopathic medicines (ie, those prepared at a potency below 24X or 12C, where Avogadro's number of molecules is 6×10^{23} , ie, equivalent to 23X or 12C). Even in immunocompromised children with radiation-induced stomatitis,¹¹⁸ homeopathic products have shown significant clinical benefits without nota-

ble side effects. As stated above, herb-drug and drug-drug interactions do not occur with homeopathy. Supporting data include an outpatient clinical observational trial in Italy. This study found an adverse event rate for 335 consecutive homeopathic follow-up visits at 2.68% (n=9 events, including one lactose intolerance reaction). The adverse events overall were rare and not severe or serious.¹¹⁹

The usual dose range below the NOAEL renders conventional toxicological reactions highly improbable, even when the original source substance may itself be an herb or mineral with some toxic potential at conventional dose exposure levels. Clinical toxicology data support this latter statement. Homeopathic medicines constitute a lower risk not only in usual clinical use but also in overdose situations. Table 2 shows data from the 2008 annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS) 26th Annual Report⁴ for categories of substances most often involved in pediatric exposures in children aged 5 years and under. It can be seen that analgesics account for 9.7%, cough and cold preparations 4.1%, antihistamines for 3.5%, and a combination category lumping dietary supplements, herbals, and homeopathics together was much lower, at 1.5%, than those three other OTC conventional drug categories.⁴

Of all exposures reported to the poison control centers for every agent, children under 6 years old were involved in only 2% of fatalities (34 of 1315 fatalities, with 75% fatal cases in adults older than age 19). The percentage of fatalities in children below age 6 related to total pediatric exposures was 26/1292754, or 0.00201%. Of the small number of reported fatalities in children (≤ 6 y old) for all types of agents, none were attributed to homeopathic medicines. On the other hand, drugs such as diphenhydramine and opioid analgesics such as oxycodone, among various other agents, were listed as factors in some of the fatalities.⁴

Clinical Effectiveness

In acute pediatric illnesses, Haidvogel et al³¹ reported the findings of an international multicenter, comparative cohort study of 1577 children with acute respiratory and ear complaints across 57 primary care

Table 2 Substance Categories Most Frequently Involved in Pediatric (≤ 5 y) Exposures (Based on Data From the Top 25 Categories⁴)

Substance Category	Number	% ^a
Cosmetics/personal care products	173945	13.5
Analgesics	125454	9.7
Cleaning substances (household)	124934	9.7
Cold and cough preparations	52723	4.1
Vitamins	50836	3.9
Antihistamines	44649	3.5
Pesticides	43526	3.4
Dietary supplements/herbals/homeopathic	19403	1.5

^a Percentages are based on the total number of pediatric exposures (N=1 292 754) in 2008.

practices. They found homeopathic treatment noninferior to conventional treatment. However, they also demonstrated significantly faster onset of improvement in children and adults with homeopathy than with conventional treatment. Homeopathy had a significantly lower adverse event rate in adults, but a similarly low rate of adverse events in children (homeopathy: 2.0% vs conventional: 2.4%, ns).

The theme of earlier onset of symptom improvements with homeopathy has replicated itself across studies in multiple countries. In a prospective observational study of 131 German children with otitis media, Friese et al also noted complete recovery at an earlier point in time for the homeopathically-treated group vs the conventionally-treated group.^{120,121} Only 4.8% of the homeopathically-treated children ended up receiving a course of antibiotics. Frei and Thurneysen had evaluated rates of improvement and costs in 230 children with AOM, treated with homeopathy versus placebo. In the latter study, they found that 39% of the homeopathically-treated children achieved pain control within 6 hours of initiating treatment, followed by reduced pain in an additional 33% after 12 hours (72% experienced less ear pain within 12 hours). The rate of symptom improvement with homeopathy was 2.4 times faster than that in placebo controls.¹²²

Following a promising randomized, placebo-controlled pilot study of individualized homeopathy in 75 children aged 18 months to 6 years,¹²³ Taylor and Jacobs recently published a study of a commercial combination homeopathic eardrop medicine for symptoms of otitis media in 120 children between the ages of 6 months and 11 years old.¹²⁴ Patients were randomized to standard therapy plus homeopathy vs standard therapy alone. They documented a faster early rate of improvement in the first few doses of treatment (directions suggest giving a dose every 4 hours until symptoms improve) in the homeopathically-treated group compared with the standard-therapy group. This finding has practical value for parents/caregivers who are unable to send their children back to day care or school until the symptoms of the infection are abated. Notably, as in earlier studies,¹²⁵ the homeopathically-treated children had significantly fewer diarrhea and “hyper” behavior adverse events than did those receiving standard care.

The homeopathic-ear drop group had antibiotic prescriptions filled only 7.1% of the time, whereas the standard therapy-alone group filled antibiotic prescriptions 36.5% of the time. The data in the Taylor and Jacobs study¹²⁴ were similar to the 4.8% antibiotic fill rate for homeopathy in the Friese et al study^{120,121} and other pilot studies¹²³ and previously published rates of antibiotic fill rates of 31% and 38% for watchful waiting prescriptions in standard therapy alone in previous studies.^{127,128}

Finally, Sinha et al¹²⁹ published a recent double-blind placebo-controlled trial of homeopathy vs conventional treatment in AOM (N=81). Both treatment groups ended up with equivalent recovery rates by the

Overview of Homeopathic Medicine Dosing^a

Homeopathic Potency or Dose	Dilution Ratio	Comment
X or D (decimal series)	1/10	Many over-the-counter acute self-care homeopathic products are low potencies (eg, 1X to 12X) with beneficial effects on local physical symptoms.
C (centesimal series)	1/100	Commonly used potencies include 6C, 12C, 30C, and 200C, for either acute or chronic conditions.
M	1/1000	Potencies such as 1M, 10M, and 50M are sometimes recommended by homeopaths in treating chronic illnesses, including systemic conditions. Higher potencies are believed to have longer-lasting effects than lower potencies. ¹³⁰
LM or Q	1/50 000	This potency series is typically administered using daily incremental dilutions and succussions at the moment of administration by the patient. Homeopaths prescribe these potencies in treating chronic illnesses, often for highly sensitive patients or those on multiple concomitant conventional drugs.

^a All remedies are prepared by triturating (grinding or milling) insoluble materials in lactose and/or diluting and then succussing (agitating) the material in ethanol-water diluent multiple times after each dilution step. New evidence indicates that succussions cause source nanoparticles (NPs) to accumulate in a monolayer at the air-liquid interface surface of the liquid, even though the concentration of the bulk form material goes down. When the top layer of succussed solution is sampled to prepare the next “dilution” step, the NP concentrations reach an asymptotic level that persist even when the bulk form dilutions have gone past Avogadro’s number of molecules (ie, 24X or 12C potencies).¹³¹

end of the study. Again, however, the homeopathy group exhibited more rapid onset of symptom improvements and much lower rates of antibiotic prescriptions (0%) than the conventionally treated group (97.5%). This efficacy study is small and needs replication, but it is consistent with the much larger body of favorable evidence on speed of improvement and reduction in antibiotic fill rates from observational and comparative effectiveness trials.

Cost Effectiveness

Most real-world outcome studies in adults and children,¹³²⁻¹³⁷ but not all,²⁸ show that homeopathy substantially lowers costs and reduces use of conventional medications in primary care populations.^{5,132} Trichard et al compared pharmacoeconomics of homeopathy vs antibiotic treatment strategies in 499 French children with recurrent acute rhinopharyngitis from a previous 6-month prospective study.¹³⁵ They found that homeopathy significantly reduced the number of episodes of rhinopharyngitis and number of complications. The homeopathic treatment group had better quality of life scores, lower direct

medical costs in charges to the public health system, and significantly less sick leave time for the children's parents (9.5% for homeopathy; 31.6% for antibiotics). Thus, in addition to faster symptom relief and cost savings, homeopathic treatment of the child markedly reduced lost time from work for parents (2/3 less sick leave time), presumably both for staying home to care for a sick child and/or from transmission of the infection from child to parent.

A different pilot observational study evaluated the addition of homeopathic treatment in recurrent upper respiratory tract infections in children below age 5 years ($N=30$ patients).¹³⁸ Primary outcome measures were the number of URIs in the 6 months prior to treatment vs number of URIs after the beginning of homeopathic care. The findings showed a significant benefit from the homeopathic treatment. Studies in adults with URIs report similar outcomes.¹³⁹ In one of the largest prospective cohort studies on patients treated with homeopathy ($N=2851$ adults and 1130 children in 103 primary care practices in Germany and Switzerland), Witt et al found major improvements in disease severity ratings and quality of life.³⁰ An 8-year follow-up study indicated that the benefits and low risks of homeopathic treatment persist long-term.¹⁴⁰

Table 3 summarizes the potential practical advantages of homeopathic care for URIs and otitis media in children. It is important to consider not only the usually lower incidence of side effects of homeopathy vs standard care in these conditions but also the low levels of reported severity and seriousness of adverse events in homeopathically-treated children. To summarize, studies indicate the potential for savings in favor of homeopathy of both time (illness time for children; parental leave time from work) and money (lower costs of symptom-relieving drugs).

Limitations

For the skeptical clinician seeking more detailed critiques of the clinical efficacy and effectiveness of homeopathy in acute pediatric infections like AOM or URIs, the reader is referred to two recent systematic

review papers available in the literature.^{93,141} For AOM and URIs, the studies, although flawed, are overwhelmingly favorable to homeopathy in terms of various practical benefits (eg, faster responses, fewer and less serious side effects, cost savings) or at least equivalent outcomes compared with standard of care.

The more recent and comprehensive review evaluated 36 different homeopathic studies on URIs and ear-nose-throat conditions.⁹³ The limitations of the available data on homeopathy are similar to those in other CAM modalities, including small samples in the controlled clinical trials, despite the positive large scale comparative effectiveness³¹ and observational³⁰ trials. Some homeopathic AOM and acute URI clinical trial studies lacked control groups, or appropriate randomization or concealment.¹⁴¹ Two negative clinical studies tested one specific homeopathic product for treating sinusitis,⁹³ but sinus infections are the not the topic here. Two other negative studies examined homeopathic treatment in prevention of flu or recurrent URIs.^{142,143} However, the present paper addresses treatment, not prevention.

The current paper does not assert that homeopathic efficacy data are strong enough for unqualified pediatric public health recommendations. Nonetheless, even a highly flawed and debated meta-analysis^{144,145} that rejected homeopathy in general acknowledged in the authors' discussion that the efficacy trial data favored homeopathy over placebo specifically in infectious diseases.¹⁴⁶ The authors of the latter meta-analysis then rejected the "quality" of the infectious disease studies, despite reporting a lack of bias and higher study quality in the homeopathic vs conventional medical studies assessed. Rather than digress into the historical controversies related to homeopathy, the present paper acknowledges the debates and limitations of the available literature but makes the pragmatic case for good real-world treatment effectiveness of homeopathy in the context of generally increased safety and cost effectiveness compared with standard care for acute, uncomplicated pediatric AOM and URIs.

Table 3 Advantages of Homeopathic Treatment Over Standard Care Alone in Previous Pediatric Research on Upper Respiratory Infections and Otitis Media

Homeopathic Advantages Over Standard Care Alone	References
Symptom improvement occurs earlier in treatment	Frei and Thurneysen 2001 ¹²² Haidvogel et al 2007 ³¹ Taylor and Jacobs 2011 ¹²⁴
Lower fill rates for watchful waiting antibiotic prescriptions 5%-7% for homeopathic care 31%-38% for conventional standard care	Harrison et al 1999 ¹²⁶ ; Friese et al 1996, 1997 ^{120,121} ; Taylor and Jacobs 2011 ¹²⁴ Sinha et al 2012 ¹²⁹
Fewer side effects and/or less serious side effects	Wustrow et al 2004 ¹²⁵ ; Taylor and Jacobs 2011 ¹²⁴
No drug-drug interactions reported	None documented for homeopathic medicines studied
Less parental sick time leave from work	Trichard et al 2005 ¹³⁵

SUMMARY

Based on the evidence, homeopathic medicines offer one viable strategy for treating pediatric AOM and URIs to reduce not only adverse events from conventional symptomatic drug treatments but also inappropriate use of antibiotics and the associated worldwide problem of drug resistant organisms. The treatment approach of homeopathic medicine focuses on stimulating the body as a complex adaptive system to overcome an infection by stimulating its own endogenous defenses. One mechanism would be as NP adjuvants for triggering enhanced immune system responses.^{70,72,77,78} As such, the clinical approaches of homeopathy and conventional medicine differ in important ways.

Nonetheless, the evidence favors pragmatic use of homeopathy in children with acute uncomplicated URIs or otitis media on the basis of greater safety, speed of onset of improvement, and cost savings. Accelerated symptomatic improvement, especially in the context of otitis media translates into the ability to reduce the use of antibiotic treatment in the early phase of illness, ie, first few days. This benefit of homeopathy is clinically meaningful for improving public health outcomes. Reducing antibiotic use in the United States and other developed countries is a public health concern in the context of a growing problem with antibiotic resistance from inappropriate and unnecessary prescriptions (<http://www.cdc.gov/drugresistance/index.html>).

It must be emphasized that this argument is given for uncomplicated pediatric cases of AOM or URIs where the primary treatment goal is symptom relief in a typically mild, self-limited infection. In contrast, the risks of more severe cases in the natural course of AOM include serious but relatively rare complications of mastoiditis, meningitis, and intracranial abscesses, as well as chronic suppurative otitis media and hearing loss.¹⁴⁷ In the latter clinical scenarios, more aggressive treatment is necessary and indicated.

In observational and comparative effectiveness studies on thousands of children from different countries, homeopathic treatment has shown low side effect rates, ie, rates comparable to or, more often, lower and less severe than those reported for conventional standard care. Preliminary indications are that homeopathic treatment may also reduce the risk of recurrent infections and lower overall costs by reducing use of conventional symptomatic drugs.

Mainstream Western medicine has an acknowledged historical bias against considering homeopathy in clinical care.^{6,148,149} The convergent clinical and basic science evidence, however, is not on the side of the skeptics in terms of the real-world utility of homeopathy. Indeed, the properties of NPs,^{15-17,150,151} complex adaptive systems models for homeopathic medicine interactions with the individual patient;^{84,85,88,92,94,108} and nonlinear dose-response effects at low doses of substances^{23,100,152,153}

Clinically Focused Resources

National Center for Homeopathy	http://NationalCenterforHomeopathy.org
Homeopathic pediatric acute care	Grandgeorge D. The homeopathy handbook for children: acutes and their homeopathic treatment. Kander, Germany: Narayana; 2012.
Homeopathic general acute care—children and adults	Jonas WB, Jacobs J. Healing with homeopathy. The complete guide. New York: Warner Books; 1996.
Homeopathic family care	Ullman D. Homeopathic family medicine: evidence based homeopathy. Available by e-book download from http://homeopathic.com (regularly updated). Lockie A. Family guide to homeopathic symptoms and natural solutions. New York: Touchstone; 1993.
Introduction to homeopathy	Lansky AL. Impossible cure: the promise of homeopathy. Portola Valley, California: RL Ranch Press; 2003. Dooley TR. Homeopathy. Beyond flat earth medicine, second ed. Timing Publications; 2002.
Conventional medical management of fever in children	Sherman JM, Sood SK. Current challenges in the diagnosis and management of fever. <i>Curr Opin Pediatr</i> . 2012;24(3):400-6.

are also emerging as major frontiers in conventional medical research.^{22,154-164} An appropriately conservative conclusion is that the effectiveness data are more extensive than the efficacy data for homeopathic medicines in AOM^{129,141} and URIs to date. Additional, appropriately-designed efficacy studies with not only good internal but also external and model validity are indicated.^{5,29,165}

At the same time, multiple clinical studies support the conclusion that homeopathy may be a pragmatic tool in clinical practice. Homeopathy has shown real-world advantages and good evidence for doing less harm than conventional treatments in these acute clinical illnesses of children. Many consumers already accept and use homeopathic medicines for self-care.^{137,166} Even assuming another completely skeptical position that the existing body of positive scientific evidence on homeopathy^{5,29} is all to be ignored and that homeopathy exerts its clinical effects solely as a “placebo” via positive patient-practitioner relationships in some conditions¹⁶⁷⁻¹⁶⁹ (though practitioners are not usually a factor in self-care homeopathy), the safety and effectiveness data reviewed above still support the pragmatic use of homeopathy over conventional OTC medications for acute symptom relief. In conclusion, to “do no harm,” practitioners have an evidence-based foundation¹⁷⁰ for taking a rational look at homeopathic medicines in acute primary care of children with uncomplicated URIs and AOM.

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Glossary of Terms

Term	Definition
<i>Bulk form</i>	The crude material form in which a substance might occur in the physical world. Most current conventional forms of drugs and raw herbs fall into the larger, bulk form size range.
<i>Complex adaptive system (CAS)</i>	A complex system is a collection of multiple interconnected parts in which the properties of the whole system are different from those of the individual parts. In a CAS, the properties reflect a dynamic, nonlinear process of adaptation to changes in the demands of the environment within which the system functions. Many natural biological and social systems are complex adaptive systems (eg, living plants and animals). The unique properties of a larger CAS system (eg, organism) emerge from the interactions of its parts (eg, cells) in space and/or time. Thus, at different levels of scale, a cell is embedded within an organism, which is in turn embedded within a larger ecosystem.
<i>Homeopathic medicine</i>	A more than 200-year-old whole system of complementary and alternative medicine in which the medicines are prescribed on the basis of their ability to match and trigger reversal of a complex pattern of symptoms (the body's "sign language") as experienced by an individual patient. A major source of debate is the nature of homeopathic medicines, which are prepared from natural plant, mineral, or animal sources by processes of trituration, followed by serial dilutions and succussions.
<i>Hormesis</i>	Hormesis involves beneficial effects at low doses (usually below the NOAEL) in contrast with adverse or toxic effects of the "same" substance at high doses. In more technical terms, hormesis is a nonlinear dose-response relationship, often bidirectional, for a given substance. Emerging research suggests that hormesis involves an adaptive response of cells and organisms to the low doses rather than a direct pharmacological effect at drug receptors.
<i>Nanoparticle (NP) form</i>	A tiny particle of a substance in the nanoscale size range (eg, from 1 to 100 nanometers in diameter, although NPs can range up to 1000 or more nanometers in diameter on one side). In the nanoscale size range, each particle acquires a large surface area to volume ratio, with properties such as increased catalytic ability and adsorptive capacity, as well as electromagnetic, thermal, optical, and quantum properties different from those of the "same" material in bulk form. Nano forms of drugs, herbs, or mineral salts can have markedly improved bioavailability, gastrointestinal absorption, and ability to cross-target cell membranes, leading to fewer side effects and lower doses to produce the "same" effect as higher doses in the bulk form of a given agent. Nanoscale forms are much closer to atoms and viruses in size than bulk forms. Recent studies suggest that, despite dilution of the bulk forms, homeopathic medicines retain persistent NP forms of their source material.
<i>NOAEL</i>	No-observed-adverse-effect level (NOAEL) is the cut-off dose for a given agent below which biologically meaningful adverse effects are not observed.
<i>Succussion</i>	A method of vigorous manual shaking or pounding of a container of liquid against a hard elastic surface to create intense fluid turbulence. In homeopathy, each dilution step is followed by multiple succussions during the preparation of a medicine.
<i>Trituration</i>	A method of mechanical crushing or grinding a bulk form material into increasingly smaller particles.

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