

Seasonal Allergic Rhinitis Study Results of Questionable Relevance to Homeopathy

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Allergic rhinitis, called hay fever when occurring seasonally, is a significant problem in many parts of the world. In this issue of *The Annals*, Kim et al.¹ present the results of a small, randomized, double-blind, placebo-controlled study involving 34 subjects and testing the efficacy of a homeopathic remedy in treating seasonal allergic rhinitis. Three standard quality-of-life measures were used to compare homeopathy with placebo. The main measurement was the self-administered Rhinoconjunctivitis Quality-of-Life Questionnaire (RQLQ) recording 28 items with responses on a 7-point Likert scale. Associated items were combined into 7 domains representing symptoms of rhinitis, and the average of the 7 symptoms was taken to represent the overall quality of life. A second measurement recorded work productivity and activity impairment (WPAI) in 4 separate domains. Finally, subjects reported subjectively on their overall health via the widely used health-related quality-of-life measure Medical Outcomes Study Short Form-36 (MOS SF-36). This consists of 36 items that were summated and averaged into 9 domains. The authors summarized their study results by saying, "Preliminary findings indicate potential benefits of the homeopathic intervention in reducing symptoms and improving quality of life in patients with seasonal allergic rhinitis in the Southwestern US."

The study is rigorous when evaluated according to Jadad et al.'s² well-recognized scale for assessing the quality of randomized controlled trials. This 3-item tool scores Kim et al.'s study at 5 out of a maximum of 5. The method of randomization was explicitly stated, giving 2 points.

The abstract stated that the study was double-blind and the methods indicated that the 2 sprays were identical, again giving 2 points. The number of people who withdrew from the study was stated along with their reasons for withdrawing, giving the maximum of 1 point.

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However, problems arise when examining the nature of the intervention tested. The particular form of homeopathy used in *The Annals'* study is called isopathy. This differs considerably from classical homeopathy, and some homeopaths do not recognize the approach as constituting homeopathy. Mitchell Fleisher,³ a member of the clinical faculty at the National Center for Homeopathy, wrote regarding another isopathy study that isopathic products (called isodes) are not administered according "to the fundamental principles of homeopathy and therefore would not be expected to work."

Homeopathy can be divided into at least 4 different types that should be differentiated in any discussion of the topic. In addition to isopathy, there is clinical homeopathy (using the same remedy for people with a similar condition), complex homeopathy (using fixed combinations of remedies for people with similar conditions, and classical homeopathy, which is the most widely used approach for chronic diseases.⁴ Central to this latter approach is the collection of detailed descriptions of the patient's physical, emotional, and mental symptoms. The correct homeopathic remedy is then chosen as one that most closely elicits the same constellation of symptoms in a healthy person. Isopathy differs fundamentally here because the allergen will not elicit any symptoms in a healthy non-allergic person and therefore fails the classical homeopathic rule cited

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by Kim et al. of *similia similibus curentur* (like cures like). According to Fleisher, this step is “of utmost importance when treating complex diseases such as asthma and allergic diatheses.”³

In contrast to Kim et al., an earlier study acknowledged that isopathy “is not usual homeopathic practice, but offers a testable model for differentiating between infinitesimal homeopathic dilutions and placebo.”⁵ These authors raise another crucial distinction that Kim et al. failed to address. Homeopathy is controversial because of the underlying belief that greater dilution conveys greater potency of remedies. The study’s introduction uses the example of a 1X dilution containing 0.1 g/mL crude medicinal substance. Such a concentration would be completely normal in a conventional pharmaceutical setting. Yet it fails to draw attention to the more usual homeopathic practice of using extremely diluted preparations. All of the earlier placebo-controlled isopathy studies used a 30C dilution.⁵⁻⁷ At this concentration (roughly 1×10^{-60} mg/mL), Avogadro’s number has been exceeded, and not one molecule of the initial allergen would be expected to remain in the solution. Yet this is the sort of concentration at which homeopathy is said to be effective, which is why it is so controversial.

Kim et al. referenced a series of 4 trials as precedent for their study of mixed allergens in homeopathic isodes for allergic rhinitis.⁶ Three studied allergic rhinitis and the fourth evaluated asthma, with all producing statistically significant benefits (although with relatively small sample sizes of 39, 144, 28, and 51 subjects). However, results from other researchers have not been positive. A placebo-controlled study with 66 patients with hay fever found no benefit at the study’s endpoint, although some benefits were apparent at midpoint.⁷ Lewith et al.⁵ used the largest sample to date (242 subjects) and failed to demonstrate significant benefits.

Since all of these studies used 30C homeopathic remedies, Kim et al.’s switch from 1×10^{-60} mg/mL to 1×10^{-6} mg/mL dilution represents a dramatic change and should have been justified. The only implicit justification given was that a 1×10^{-6} wt/vol dilution is a standard immunotherapy dose. However, conventional immunotherapy uses these concentrations in injections, raising questions about the validity of comparing this study with immunotherapy. At the same time, its connection with classical homeopathy, or even the previous isopathy literature, is tenuous at best.

Problems regarding the nature of the test remedy do not address the findings that significant improvements were reported. These require closer examination of the statistical analysis. The 3 questionnaires were administered to each subject at baseline and 4 weeks later. The differences between baseline and post-treatment measurements were obtained for each subject. The average and standard deviation were recorded for each domain. The differences between the domains at the beginning and end of the study were measured and tested for significance using Student’s paired *t*-tests of mean differences.

The so-called “Student *t*-test” was devised in 1908 by William Gosset to tackle the problem of small sample comparisons. At the time, Gosset was working in the Guinness brewery in Dublin, and his conditions of employment resulted in his being unable to openly claim credit for his findings. Hence, he styled himself with the name Student.⁸ Gosset’s *t*-test is predicated on 2 assumptions: that the data are measured on a continuous scale and that they come from a normal distribution.

The Likert scale is neither continuous nor normal. It is an ordinal measure used to assess feelings, opinions, and attitudes. It presents a set of attitudes, and subjects are asked to express agreement or disagreement on a discrete scale. Each degree of agreement is given a ranking. Even though data measured on a Likert scale are far from continuous, it is common practice in the social sciences to apply *t*-tests. In defense of Kim et al.’s use of *t*-tests, it could be argued that the domains or summated scales used, which consist of summing and averaging a set of associated items, are less discrete than the variable that would have been obtained if single items had been analyzed.

The *t*-test is robust in the sense that small departures from normality do not affect the validity of the results.⁹ However, *t*-tests may yield inaccurate results, and the statistical significance may be less than that reported if the data are nonsymmetric or skewed. Studies with samples as small as those used here (18 in the homeopathic group, 16 in the placebo group) should therefore provide frequencies and bar charts to allow examination for skewed results. A coefficient of skewness of the data could also be recorded. In cases where measurements were not deemed to be sufficiently symmetric, the nonparametric Wilcoxon signed-rank test for paired comparisons would have been a better alternative. Other descriptive statistics, such as minimum, maximum, median, and interquartile range, would improve our understanding of the data.

While the authors report that they estimated their sample size using 80% power to detect an actual change of 30% improvement, such calculations are based on normality assumptions that are not applicable to Likert scales. Since the samples are small, it is unlikely that the power claims are valid.

Other data that could have been reported to allow a clearer, more transparent understanding of the significance of the results include the means and standard deviations in MOS SF-36 and an overall average representing the total symptoms—as was given for the RQLQ domains. The authors do not report Cronbach’s α coefficient for internal consistency and reliability of the domains, but may have justified this since these scales have previously been validated.

The results from the *t*-tests should be looked upon as indications of possible differences or trends rather than definite results, with further investigation needed for confirmatory analysis; indeed, the authors themselves make this reservation. The tentativeness of any conclusion is additionally warranted when the overall results are examined. In the 2 self-administered questionnaires (RQLQ, MOS

SF-36), the mean changes are positive for all domains for both the homeopathic and placebo groups. The authors' conclusion that "scales from the RQLQ, MOS SF-36, and WPAI questionnaire showed significant positive changes from baseline to 4 weeks in the homeopathic group compared with the placebo group" does not give the full picture since significant positive changes, albeit fewer, were also observed in the placebo group, and many of the changes observed in the homeopathic group are not significant.

General concerns about the appropriate design and analysis of homeopathic trials have been documented. One meta-analysis concluded that the results of homeopathy trials could not be explained solely on the basis of a placebo effect.¹⁰ However, when the same authors reexamined the same data, they found "clear evidence that in the study set investigated more rigorous trials tended to yield smaller effect."¹¹ They concluded that bias was the most plausible explanation.

Kim et al. present us with another small trial with somewhat significant results. Technical questions about the appropriateness of the statistical analysis aside, more practical questions must be raised about the clinical significance of the results. The biggest question is, just what did the researchers test? The nasal administration of allergens for only 4 weeks is not conventional immunotherapy.¹² The dose used was in the same range as that used parenterally in immunotherapy, which is immensely higher than that used in previous isopathy studies and takes the remedy out of clearly homeopathic concentrations. Classical homeopaths will also question the lack of detailed symptom collection and treatment not being individualized. Whatever caused the alleged benefits reported here should not be called homeopathy.

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References

1. Kim LS, Riedlinger JE, Baldwin CM, Hilli L, Khalsa SV, Messer SA, et al. Treatment of seasonal allergic rhinitis using homeopathic preparation of common allergens in the Southwest region of the US: a randomized controlled clinical trial. *Ann Pharmacother* 2005;39:617-24. DOI 10.1345/aph.1E387
2. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJM, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Controlled Clin Trials* 1996;17:1-12.
3. Fleisher MA. Homeopathy or isopathy? (letter). *J Fam Pract* 2002;51:984-6.
4. McCarney RW, Linde K, Lasserson TJ. Homeopathy for chronic asthma. *Cochrane Database Systematic Rev* 2003, issue 4. CD000353.pub2. DOI 10.1002/14651858.CD000353.pub2
5. Lewith GT, Watkins AD, Hyland ME, Shaw S, Broomfield JA, Dolan G, et al. Use of ultramolecular potencies of allergen to treat asthmatic people allergic to house dust mite: double blind randomised controlled clinical trial. *BMJ* 2002;324:1-5.
6. Taylor MA, Reilly D, Llewellyn-Jones RH, McSharry C, Aitchison TC. Randomised controlled trial of homeopathy versus placebo in perennial allergic rhinitis with overview of four trial series. *BMJ* 2000;321:471-6.
7. Aabel S, Laerum E, Dolvik S, Djupesland P. Is homeopathic 'immunotherapy' effective? A double-blind, placebo-controlled trial with the isopathic remedy *Betula 30c* for patients with birch pollen allergy. *Br Homeopath J* 2000;89:161-8.
8. Student. The probable error of the mean. *Biometrika* 1908;6:1-25.
9. Jacqui J, Wan CK. LISREL approaches to interaction effects in multiple regression. Volume 114: quantitative applications in the social sciences. Thousand Oaks, CA: Sage Publications, 1996.
10. Linde K, Clausius N, Ramirez G, Melchart D, Eitel F, Hedges LV, et al. Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials. *Lancet* 1997;350:834-43.
11. Linde K, Scholz M, Ramirez G, Clausius N, Melchart D, Jonas WB. Impact of study quality on outcome in placebo-controlled trials of homeopathy. *J Clin Epidemiol* 1999;52:631-6.
12. Winther L, Malling H-J, Mosbech H. Allergen-specific immunotherapy in birch- and grass-pollen-allergic rhinitis. II. Side-effects. *Allergy* 2000;55:827-35.